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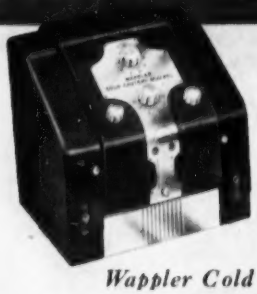

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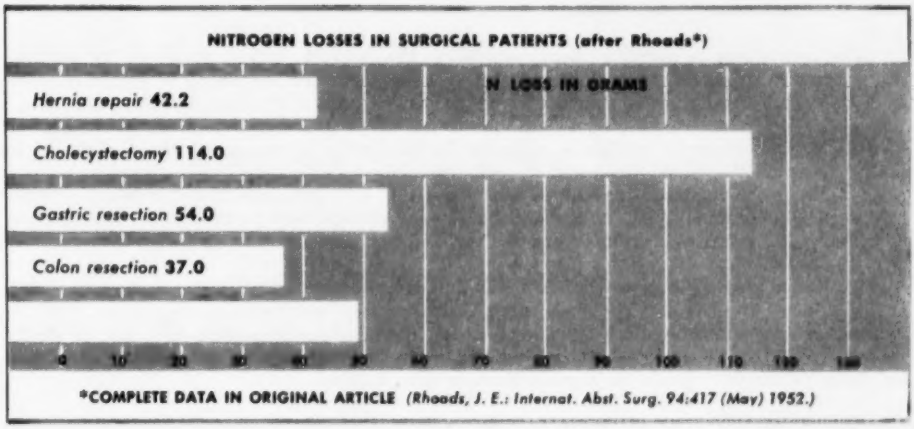
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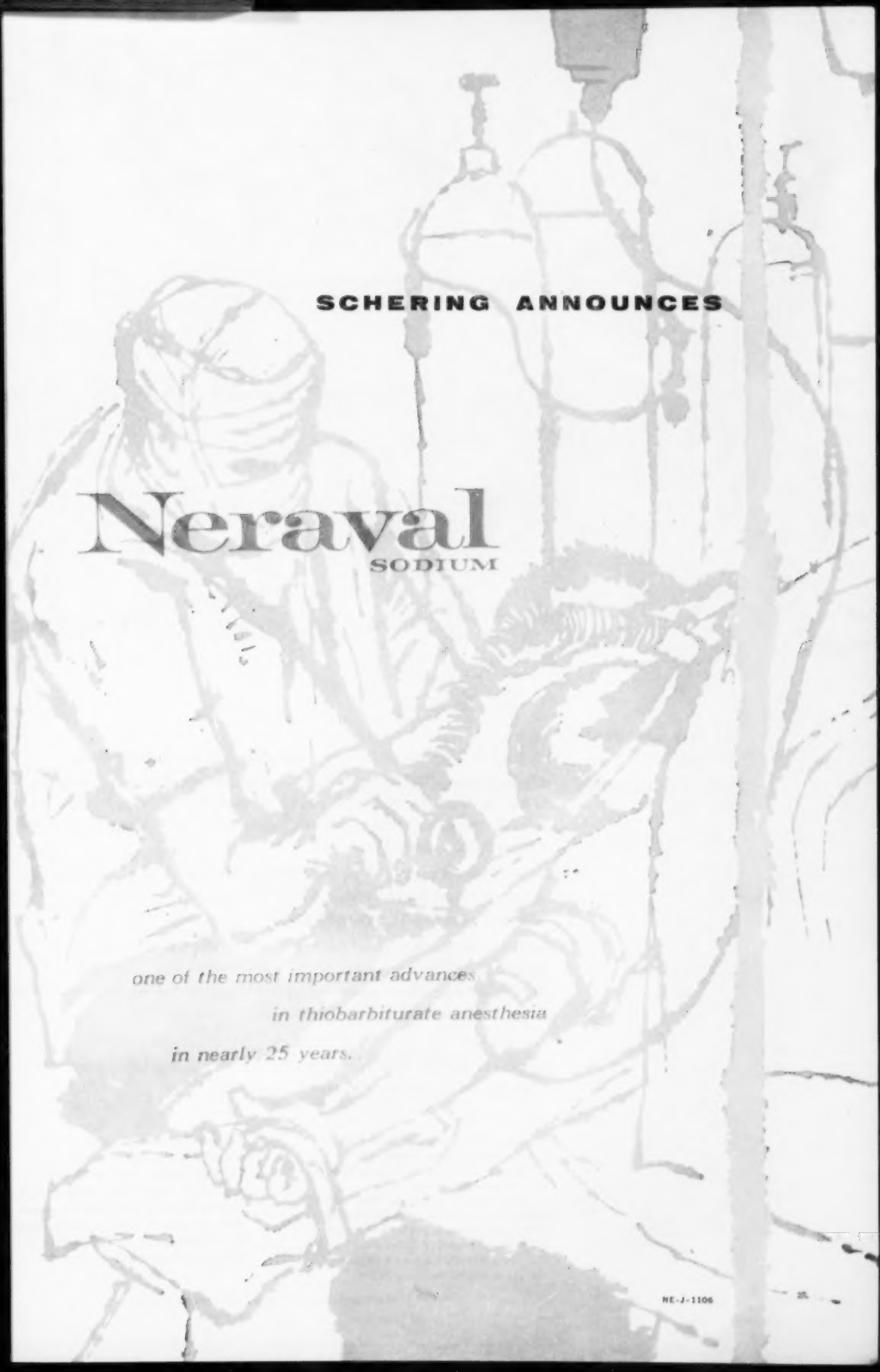
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Indications for Surgical Intervention in Regional Ileitis

BURRILL B. CROHN, M.D., New York

An audible tendency exists to disparage the value of surgery in the treatment of regional ileitis. The percentages of recurrences after operation are played up; the fact that surgical procedures serve often as long-term palliative factors is forgotten or not sufficiently emphasized. Operative intervention is often inordinately delayed in order to wait for a "better timing" and to allow Nature to heal a spontaneously incurable malady. The pendulum has swung too far to the right in my own estimation. It is therefore timely to reconsider the life history of the disease—what happens when the malady is allowed to run its natural course—and the success in whole or in part of surgery, or perhaps its failures.

Originally,[1] as described, most of the cases were—and they still remain—in the highest percentage of instances a disease process involving 8, 10, or 12 in. of the distal ileum. Historically the earliest success in treating this type of disease was by resection as soon as the diagnosis was reasonably established. With the advent of the recognition of ileojejunitis a few years[2] later it became obvious that not all cases of enteritis were responsive to large-scale extensive resection. Beginning in 1939,[3] it was held that a short-circuiting procedure could be accomplished with greater facility, with less operative mortality, and with equally good end-results.

The original rate of recurrences after operation was first recognized and cited at 10.15%.[4] As more time passed and more extended follow-up was accomplished, this figure was successively raised to 22.5%, 35%, or even higher by some authorities; hence a tendency arose to discountenance all surgical procedures except those for obstruction or for intractable fistulas. Just what are the merits of the case; where should a clinician strike a balance?

Medical Treatment of Regional Ileitis

Is there an adequate and satisfactory conservative method of treatment for regional ileitis? None that I know of. In a review of my, by now, almost 700 cases, an occasional case, perhaps 10 in all, may be said to have accomplished a spontaneous recovery. Most of these cures are instances of acute regional enteritis which proceed to self-healing without a transition to the chronic granulomatous phase of the disease. Nor are we considering here the instances of diffuse ileojejunitis in which the upper small bowel shows much greater ability to heal and resolve than does the terminal ileum when affected by the disease. The cases of true regional or terminal ileitis which spontaneously recover, achieve a negative radiogram, and avoid complications can be counted on the fingers of two hands.

Submitted for publication Nov. 2, 1956.

From the Department of Medicine, Mount Sinai Hospital.

Just what is this medical treatment of regional ileitis? Supportive treatment; high-protein diet; vitamin replacement by oral or, better, intramuscular administration; much physical rest. Radiotherapy has been tried but is inconclusive in its results, to say the least. It has been suggested that we are dealing with a psychosomatic disease. Such studies as have been made with control series of persons have failed to substantiate such a hypothesis. My own conscious observations do not tend to affirm any psychosomatic factors in the causation or aggravation of the disease; certainly I have never seen psychoanalysis or psychotherapy achieve any singular beneficial result.

Antibiotic therapy is restricted to its employment against suppurative complications, mainly in the nature of localized peritonitis where internal intestinal fistulas or external perirectal fistulas do exist. Antibiotics are useless against diarrhea and often cause its aggravation by untoward bacterial reallocations.

Steroid therapy offers the best approach to specific therapy. While a corticosteroid deficiency has as yet not been demonstrated, the beneficial effects of steroid therapy, at first hesitatingly asserted,[5,6] have later been more enthusiastically upheld.[7,8] The dramatic and convincing effect of corticotropin (ACTH) as seen in cases of ulcerative colitis, particularly in its acute severe febrile phase, cannot be reproduced in ileitis; yet large, often massive, doses of corticotropin and cortisone in the latter malady give very promising clinical results—temporary perhaps, curative questionably. Dosage must be large and should be continued over long periods of time. The Cushing syndrome occurs rarely; intestinal perforation or hemorrhage, never, in my experience, though such accidents have been reported.

Since, therefore, spontaneous healing by natural means is remote and rare, and in view of the fact that there exists in our armamentarium no adequate conservative medical treatment, then what are the indications for, what are the virtues of, surgical intervention, and what are the late results of radical intervention?

Contraindications to Surgery

Let us first exclude types of cases for which surgical intervention is contraindicated.

1. *Extensive Ileojejunitis with Diffuse Involvement of the Whole or Large Part of the Small Bowel.*—A few cases of massive resection have been reported in the literature, some with apparent success even though only a few inches of proximal jejunum remain anastomosed to the colon. These cases are few and far between, and such a stupendous undertaking should not be lightly considered. When obstructive manifestations occur in high ileojejunitis, localized short-circuiting procedures become mandatory and are highly successful.

2. *Acute Ileitis.*—The abdomen should never be entered in acute regional ileitis if the diagnosis can be preoperatively determined. Here acute abdominal disease is nearly always accompanied by diarrhea; vomiting is absent. But if because of the warrantable suspicion of acute appendicitis laparotomy is undertaken, then let the surgeon beware; undertake no resection or short-circuiting procedure and leave the abdomen as rapidly as possible. Practically the only mortality ever seen in ileitis is where a brash surgeon undertakes a resection in the face of an acute fulminating regional ileitis. Whether to remove the appendix or not is a moot question. Acute suppurative appendicitis does occur sufficiently often, not as a complication of but as an incident to ileitis, to warrant an appendectomy, if such can be easily accomplished. The fact is that in 25% of the cases of ileitis appendectomy has at some previous occasion been accomplished but without altering the clinical life history of the disease. It does not, however, seem that appendectomy increases the tendency toward abdominal-wall fistula to the anterior parietes.

3. *Mucosal Type of Enteritis.* — One must exclude also from surgical intervention such cases of so-called "mucosal type" of enteritis in which the disease originally involving only the distal small bowel extends rapidly in an orad direction, eventually to affect the whole ileum and jejunum; fortunately this type of case is extremely rare.

4. *Combined Ileocolitis.*—Cases of combined ileocolitis in which both ileum and colon are affected, either originally (synchronous) or later (metachronous) should be excluded, since this very complicated and bewildering combination of two disease processes calls for individual judgment. To consider the relatively simple problem of surgical treatment of regional or terminal ileitis at the same time with combined ileocolitis is to compound confusion.

Positive Indications for Surgery

1. *Localized Regional or Terminal Ileitis*

Considered first is ileitis with a lesion restricted to the distal small bowel involving 8 to 12 or slightly more inches just proximal to the ileocecal valve; skip-lesions are not demonstrable by radiographic interpretation. The course of the disease in this type of case is persistent and chronic; a mass is palpable in the right lower quadrant; secondary anemia is present; fever, mild but continuing, is observable, and diarrhea and abdominal cramps are severe and recurrent. On careful survey of the radiographic films, internal fistulas from small bowel to neighboring viscera are discernible. These fistulous tracts lead from ileum to ileum, to various segments of other small-bowel loops, to colon and sigmoid, to Fallopian tubes or uterus. Occasionally these internal fistulas invade or threaten to invade the urinary bladder, ureters, or urethra in the male. True penetrating urinary vesical fistulas are rare, but multiple tiny incomplete fistulas are common.

Given a mass, fever, diarrhea, pain, internal fistulas, and a lesion localized to the terminal ileum, the indications for operation are evident.

2. *Fistulas to the Abdominal Wall.*—These fistulas from diseased porous ileum to the anterior abdominal wall, to the posterior parietes, to the inguinal regions, or even to the anterior facies of the thighs are frequent. They most frequently follow the scar of a previous laparotomy, but not necessarily so. They are mildly purulent, at times contain fecal material, constitute a source of great annoyance to the patient, and cause depletion of nourishment and weight loss. They represent also an irreversible process unless operation is performed.

3. *Perirectal Fistulas.* — These fistulas originating in ischiorectal abscesses, rectal fistulas, and rectovaginal fistulas are pathognomonic of true inflammatory intestinal disease, both ileitis and colitis, but predominate in regional ileitis. Local excision of such fistulas is impossible and unsuccessful in the face of intestinal disease higher up. They too represent an irreversible complication as long as the original ileitis remains as an active disease, but they heal spontaneously, like the abdominal-wall fistulas, once the original site of the disease in the small bowel has been resected or short-circuited.

4. *Hemorrhage.*—This indication occurs rarely, in about 5% of all cases, either as an initial symptom or as a late complication of an advanced disease. The hemorrhage occurs practically always as gross bleeding per rectum, very rarely as hematemesis. It occurs also as a complication of recurrent ileitis, after unsuccessful attempts at previous surgical procedures. The hemorrhage is often profuse, rarely massive, and usually ceases spontaneously, but it constitutes a true indication for surgery.

5. *Intestinal Obstruction.*—This indication for surgery is usually a late manifestation of the disease and portrays an attempt at healing with scarring and resultant contraction of the lumen of the bowel. Obstruction may represent an acute exacerbation in a previously long-existing lesion or a result of progressive self-healing with scarification. Intestinal obstruction as an

early or initial symptom of regional ileitis is rare but may occur. Obstruction in localized loops of high ileum or jejunum calls for surgical treatment in the form of short-circuiting procedures. Segmental resections in the face of obstruction are usually inadvisable unless fistulas to the abdominal wall exist.

Localized involvement of the duodenum, usually in the third and fourth portions, frequently causes postpyloric obstruction and necessitates gastrojejunostomy, a procedure which is usually curative.

6. *Recurrent Ileitis.*—Ileitis which recurs after a previous surgical procedure (resection or short-circuiting) is usually a medical rather than a surgical problem. But where the diarrhea is excessive, where the state of the body nutrition is seriously impaired, where electrolyte imbalance is present or is imminent, where gross hemorrhage or obstruction occurs—in other words, where medical conservative management of the recurrence fails—then surgical intervention is again justified and warrantable.

7. *Persistent Activity in Primary Lesion After Attempted Short-Circuiting Procedure.*—Those surgeons who favor a palliative single-stage short-circuiting ileocolostomy with transaction of the ileum are occasionally faced with continued activity at the original site of the regional or terminal ileitis. Fever may continue; a painful mass constituted of loops of small bowel matted together by a fistulous tract may remain as a painful focus of infection and the site of advancing fistulous tracts. Not very often, but occasionally, it is necessary to enter the abdomen at a later moment and to resect the original point of granulomatous involvement.

8. *Perforation.*—Free perforation of ileitis into the peritoneal cavity never occurs, or at least I have not seen it. Localized walled-off gradual perforation with the formation of a mass surrounding a purulent cavity does occasionally occur and constitutes a situation which calls for surgical intervention.

Timing of Original Surgical Attack

When is the optimal time to operate in regional or terminal ileitis? The first cases originally described were purely local and terminal in their anatomical site, and, most of them having been of long standing and having remained localized, resection was eminently successful and gave rise to the impression that operative intervention was indicated as soon as the diagnosis was made. With more experience over the next two decades and with the consciousness of a high and increasing percentage of postoperative recurrences, the disappointment had or has led to a second look, a wariness rather than a brash approach, and a tendency to delay. The theory back of this delay was to seek a moment for surgical intervention when the inflammatory process had "quited down," had become more localized, had entered a sclerotic phase rather than an ill-defined mucosal infiltration without discernible or easily recognizable upper limits of involvement. Whether this often inordinate delay has led to a lower rate of postoperative recurrence is to my mind and experience a doubtful fact. On the other hand, much of this irresolute "marking time" merely prolongs the painful and debilitating aspects of the disease; it creates often an unhappy state of mind in the patient who lives suspended in doubt, having been told that operation is nevertheless the eventual solution of his illness. The time to operate is when a course of conservative therapy, supportive, steroid, and antibiotic, has been given ample time to convince one that nothing further is to be gained by delay. During this period, presumably, successive radiographic studies will have demonstrated the fact that the lesion in the bowel is static and has failed to extend upward beyond the recognizable skip-lesions. This is the usual rule in the life-history of this disease, except in the rare "mucosal" type where rapid extension and recognizable upper limits are impossible of ascertainment. The longer one now delays the greater is the invitation to more anatomical extension, to

internal bowel fistulas, and to perirectal complications. Cases of long standing with protracted clinical histories are appropriate to early surgery; recent subacute cases call for more study and a delayed reaction to operative interference.

Type of Operative Procedure.—We in our institution, and I believe most of the surgeons throughout the country, prefer a short-circuiting of the lesion by ileocolostomy, with a transection of the ileum 10 to 18 in. above the uppermost point of upper discernible affection of the bowel. Yet there are many centers of learning and practice in which resection of the lesion is still preferred. Originally the mortality of radical resection was considerably higher than that of a short-circuiting procedure;[4] today the palliative procedure can be performed with practically no operative mortality, and the risk of primary resection is reduced to a minimum of 2.3% (Van Patter et al.[9]) Whether the rate of recurrence of the lesion in subsequent months or years is greater with one type of procedure than the other is questionable. The extensive study at the Mayo Clinic as published in 1954 gives an approximate recurrence rate of 54.5% for exclusion cases (a small series of cases only and therefore possibly not finally accurate) and a higher rate (66%) of recurrences in a larger group of cases of primary resection.[9] The operative mortality of resection being greater and the end-results being no better than those of short-circuiting, to say the least, where then is the logical scientific preference for resection?

In any case it is generally accepted that transection of the ileum above the affected loop of bowel is mandatory, in order to localize the lesion and prevent subsequent upper extension of the disease. Exceptions to this rule are rare and occasional and probably depend on special circumstances. In most instances if symptoms persist the simple procedure of subsequently transecting the ileum above the lesion in the distal bowel is immediately curative.[10]

The type of anastomosis of ileum to colon varies with individual surgeons. Many prefer the end-to-end anastomosis, which seems logical because with this procedure one averts possible later complications in the blind loop. The side-to-side anastomosis seems simpler and less likely to have leakage at the site. Actually the blind loop rarely gives trouble; occasionally the blind end may be the site of severe hemorrhage or of distention with rotation and obstruction, but these are very rare and late complications if they do occur.

Massive resections of the whole ileum with at times large segments of jejunum constitute a desperate venture and an attempt at a lifesaving procedure in the face of a steady downhill course of the patient who suffers a diffuse ileojejunitis. Remarkably, many of such patients survive the extensive resection, most of them with moderate or marked nutritional and electrolyte imbalance. Some, however, with only a few inches of remaining upper jejunum, do well and maintain controlled bowel movements and preserve a good state of nutrition.[11]

Postoperative Recurrent Ileitis.—The actual true rate of recurrence of ileitis after the conventional and accepted methods of surgical intervention is difficult to evaluate. This rate may vary from 22.5% in our series as published in 1951 to an anticipated recurrence rate of 30% at the Lahey Clinic[12] (1955, Marshal and Mathieson), to 58% at the University of Pennsylvania (Dyson, Hodes, and Rhoads, 1954[13]), to 54.5% to 66% at the Mayo Clinic.[9] These figures on the face of it are truly disconcerning, but they represent only a statistical statement of fact, and statistics in themselves without amplification do not necessarily tell the whole truth. An important suggestion has been made by the group study from the University of Pennsylvania.[13] These authors suggest that a distinction exists between "clinical" and "radiological" recurrences. Their percentage of "clinical" recurrences is far below that of so-called "radiological" re-

currences, the idea being that a slight irregularity in the mucosal pattern of the "new" terminal ileum after operation does not necessarily imply that a true clinical recurrence is present. It will be interesting to follow up this suggestion to determine whether a differentiation of value has appropriately been made. At the moment it is my own impression that a radiologic demonstration of recurrence is followed sooner or later by clinical symptoms; the time lag between the two may be significant. The largest percentage of recurrences take place in the first 6- to 12-month period after operation (60%),[9] but late recurrences may be noted as long deferred as 11, 14, 17, or 21 years after the operation. The difficulty of truly evaluating the rate of recurrences is complicated by the fact that many of them are tabulated many years after the surgical intervention. Let me illustrate this fact by the following brief history. Case 1 in my original series underwent resection for terminal ileitis by Dr. A. A. Berg in 1930, and for all these years his case constituted my joy and satisfaction in that I had restored him to health. The follow-up in his case was uniformly one of perfect well-being and 100% of efficiency. A few months ago, in 1956, he returned with complaints for the first time of mild diarrhea; a radiographic study revealed a short localized area of recurrent ileitis. For 26 years this now middle-aged man had been apparently perfectly well. Such an incident points out two lessons: one, that in the intervening span of 26 years his health, like that of so many with late recurrences, had been fully restored in the interval; two, that the longer years of follow-up the higher will eventually be the rate of disappointing recurrences. But are not 11, 14, 17, 19, or 26 years of good health a satisfactory return from an operative procedure? As a palliative step such an operation warrants confidence and satisfaction, even though the late "up-state returns" upset the anticipated more favorable poll.

Nor is the fate of the case of recurrent ileitis often such an unhappy one. Complications in the form of fistulas are usually eliminated, diarrhea as is usual with ileitis is not severe, nutrition is customarily fairly well preserved, secondary anemia is moderate. Most cases of recurrent ileitis do not require any secondary operative procedures and can be carried along under conservative medical therapy. Attempts to salvage the situation by secondary surgical intervention lead again to later recurrences; hence, tertiary operations are again invited, always with disappointing results. Special situations such as hemorrhage or obstruction or persistent fistulas are an exception to the rule, and here operative interference becomes mandatory.

In the light of our present-day knowledge of the life history of this disease with its recognized anatomical distribution and its known skip-lesions, considering that the operation is undertaken by experienced and competent surgeons who at the operating table can identify the upper limits of the pathological process, why then the high rate of recurrences? This is a most difficult question to answer. The surgeon at the time of operation will hopefully anastomose a healthy ileum (demonstrated by biopsy to be free of disease) to a healthy colon, again free of disease, and yet recurrence of the ileitis is likely. Take down this recurrent ileitis and again, as a teritary procedure, anatomose new healthy ileum to healthy colon, and the chances are very great that recurrence will again take place in the "new" terminal ileum. This same area of ileum if it had been left alone would have remained free of disease for an invariable period of time; anastomose it to the colon and disease appears. What is it that occurs to create a recurrent malady when healthy ileum and healthy colon are so juxtaposed? Does the surgeon by so doing recreate the relationship of terminal ileum to the cecum as seen normally anatomically, the ileocecal valve being apparently no bar to the disease? Perhaps biological or bio-

chemical factors, or enzyme relationships, or myenteric neurological factors play a determining role.

The recurrence is always in the ileum, practically never in the colon, which seems to have an immunity to the disease except in that much smaller group of cases of combined ileocolitis. Some of the newer research observations may afford a clue; they certainly give rise to thoughts. Brunner-like glands have been observed in the mucosa and submucosa of the resected ileum in cases of ileitis, glands similar to those appearing normally in the duodenum and pylorus.[14] Sixteen of thirty-four resected specimens of ileitis studied histologically showed these Brunner-like glands, and most of these cases were followed by recurrent disease.

In the other 18 cases these glandular acini were not demonstrated in the resected specimen, and in these instances recurrent disease was absent.

Comparative studies have been made of the number of ganglion cells in the myenteric plexuses of the normal bowel as compared with those of regional ileitis.[15] "Persons suffering from regional enteritis possess in the myenteric plexuses of the small intestine approximately three times as many ganglion cells as persons not so afflicted" (Davis, Dockerty, and Mayo). Regional enteritis of long duration is attended by a greater increase in ganglion-cell counts than disease of short duration.

There may be only partial or doubtful significance in studies such as these; for the changes may be secondary rather than in any way causative to the disease. But it is probable that along these lines or by extension of biochemical research both the cause of the disease and the explanation of postoperative recurrences may be found.

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Propantheline Bromide (Pro-Banthine), an Adjuvant in the Treatment of Pancreaticoduodenal Fistulas

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The leakage of pancreatic juice is a very serious complication in the early postoperative course of the gastrectomized patient. Martin,[1] reporting on some 520 consecutive gastrectomies, found one true pancreatic fistula, which was fatal, and five pancreaticoduodenal fistulas, four of which were terminated by death.

Bonniot,[2] discussing the etiology of this type of fistula, suggests that at least some may be pancreatic in origin. He points out that it is practically impossible to resect a posterior duodenal ulcer without at least minimal damage to the pancreas. Minor damage to some acini may result in leakage of pancreatic juice around the duodenal stump with consequent digestion of the suture line. In discussing the same problem, Lahey,[3] Bartlett,[4] and Cedermark[5] have presented anatomical evidence that direct damage to the main excretory ducts of the pancreas is very likely to occur in difficult dissections of posterior penetrating ulcers.

The ultimate fate of these fistulas is variable. Some patients do not survive the early stages.[1,6] Others develop a chronic fistula which in time requires further surgery.[3,4,7,8] Finally it is claimed that in the majority the fistulas will close spontaneously.[8-12]

In view of the complexity of the mechanisms which regulate the secretory activity of the pancreas, we believe that pancreatic fistulas which follow gastrectomy with gastrojejunostomy should be considered separately from fistulas where the continuity of the upper gastrointestinal tract has not been altered. Pancreatic juice is produced by means of two different types of stimuli. By one such stimulus the release of pancreatic juice is secondary to hormonal stimulation. The source of the hormone is the duodenal mucosa, which liberates it in the presence of an acid duodenal content. As the pancreatic juice neutralizes the acidity of the duodenum, less and less hormone is released until a complete suppression is reached. Secondly, pancreatic juice is produced through vagal stimulation, and this stimulus is independent of digestive processes. It has been shown that the two stimuli will result in the production of different types of pancreatic juice.

The typical patient with a pancreatic fistula following gastrectomy will continuously lose water, electrolytes, and proteins. This fluid loss is considerable and has been variously estimated between 500 and 1500 ml. per day. In the case reported by Cedermark[5] the fluid loss was as much as 2300 ml. every 24 hours. The pattern of electrolyte loss may be visualized easily if it is recalled that the pH of pancreatic secretion is approximately 8.0 and that its alkalinity is due largely to the presence of sodium bicarbonate. Therefore, the fluid loss results in sodium depletion compounded by pronounced dehydration.[13] In addition, the matter of protein loss has been considered in our cases. After gastric resection, if the gastrojejunostomy is functioning properly, there can be no acidification of the duodenal content. Hence, the hormonal mechanism of pancreatic secretion is depressed or even suppressed. Whatever pancreatic juice is produced then results mainly

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from vagal stimulation. According to Starling,[14] pancreatic juice collected after injection of pilocarpine contains 4.8 gm. of protein per 100 ml. Thus, a 1500 ml. fluid loss through a fistula would result in a loss of 72 gm. of protein. This loss should be compounded through an additional protein loss resulting from digestion of the wall of the fistulous tract and of the surface of its orifice. Finally, the low protein intake of the gastrectomized patient during the early postoperative period makes the replacement of these protein losses difficult.

Since C. Bernard observed pancreatic atrophy following the intraductal injection of olive oil, a number of attempts have been made to reduce pancreatic secretion. Wolgemuth[15] advocated a diet which was low in carbohydrate content and high in protein and fat, although Kroiss[16] doubted the value of such a diet. Since it has been observed that dehydration affects pancreatic secretion,[17] deliberate dehydration has also been advocated. Cedermark[5] reports only minimal effects after dehydration, and it appeared unwise to us to deprive of water a patient who is losing such large amounts of body fluids.

Even though the majority of fistulas will close spontaneously and those secondary to gross injury of the main pancreatic ducts will require later surgical correction, still it appears reasonable that any measure which will effectively reduce or suppress pancreatic juice formation will greatly simplify the management of these fistulous patients. Atropine has been advocated as a vagus-inhibiting agent capable of blocking pancreatic secretion,[18] although its use has been disappointing.[3-19] With the introduction of methantheline bromide (Banthine) a new drug was made available which could be useful in this particular situation. The experimental work on animals of Thistlethwaite[20] and of Howard[21] and Whitrock[22] in man indicated that methantheline bromide effectively reduces pancreatic secretion. Shingleton,[23] working on experimental acute pancreatitis, concluded, indirectly, that methantheline bromide reduces pancreatic secretion, and Warren[8] suggested that this drug be tried in patients with pancreatic fistulas. Annis,[24] however, found that the effective dose of the drug was so great that side effects prohibited its use. With the introduction of propantheline bromide a more specific drug with diminished degree of side effects has been made available. This fact, combined with an assumption that pancreatic secretion is mostly vagal after gastrectomy with gastrojejunostomy, led us to use propantheline bromide in two patients. The results have been very encouraging, and our observations are reported below.

CASE 1.—A 63-year-old man was admitted to the Ellis Hospital with chief complaint of profuse melena. An ulcer history of about 20 years' duration was obtained, with numerous bleeding episodes in the last 10 years. He had been hospitalized at the time of each of these episodes but had always refused operation. The patient had been on an ambulatory ulcer diet for a considerable period of time with only moderate relief of symptoms. His systolic blood pressure was 95, the pulse rate 80, the rectal temperature 37 C. Aside from pallor and weakness, no other positive physical findings were present. The peripheral blood showed a hemoglobin content of 6.0 gm. per 100 ml., and the packed cell volume was 20%. Immediate blood replacement therapy was instituted, but the patient made very little progress during the next three days, and on the fourth day a subtotal gastrectomy was performed. A duodenal ulcer, which had eroded into the head of the pancreas, was found, and after the duodenal stump was freed a satisfactory closure was performed. An antecolic end-to-side gastrojejunostomy was then completed. Bleeding from the ulcer bed in the head of the pancreas had been more or less persistent throughout the procedure, and numerous attempts at controlling this bleeding had been unsuccessful. In the course of a final attempt to control it, the bleeding became unmanageable and it was decided to pack the ulcer bed tightly with sponges and close the abdomen. The immediate course was satisfactory, although mild icterus of the sclerae appeared on the second day. By the fifth day, typical manifestations of obstructive jaundice were present and reoperation considered mandatory. At this time all sponges and clamps were removed without any hemorrhage. Extensive necrosis of the pancreatic tissue was present, and all of the tissues and organs of the upper abdomen were conglomerated into a solid mass. The gallbladder

was very tense, and calculi were palpated within its lumen. A cholecystostomy and removal of the calculi was performed as a palliative measure. No persistent attempt was made to demonstrate the common duct. Drainage from the cholecystostomy tube was satisfactory, and three days later it appeared to be lessening. However, at that time profuse pancreatic secretion began draining around the cholecystostomy tube. During the next four days, the amounts of fluids and electrolytes lost became a serious problem and the maintenance of an adequate balance almost impossible. Dressings required changing every two or three hours because of the profuse drainage, and the skin around the fistulous orifice showed signs of enzymatic digestion. On the fourth day after the development of the fistula the intramuscular administration of propantheline bromide, 15 mg. five times daily, was begun. Within a few hours after the administration of the first dose the amount of drainage was reduced. Within 48 hours the drainage was "scanty," and on the seventh day after the onset of the propantheline bromide therapy the drainage had ceased. The drains and the cholecystostomy tube were removed, and the patient was sent home without dressings on the 17th day after the fistula had developed. He was readmitted 10 months later because of a cicatricial stenosis of the common duct. An exploration was performed; the common duct was demonstrated and reimplanted in the duodenum. His postoperative course was uneventful, and he is in good health at the present time, 18 months after the choledochoduodenostomy.

Case 2.—A 55-year-old man was admitted with chief complaint of hematemesis, weakness, and dizziness. Within an hour after admission, a large amount of dark blood was evacuated by rectum. When questioned, the patient disclaimed a history of ulcer, previous hemorrhagic episodes, previous surgery, and serious medical illness. The systolic blood pressure was found to be 95, the pulse rate 115, the oral temperature 38 C. He was not in obvious distress, and, aside from mild pallor, the physical examination was essentially negative. Within 12 hours after admission he had received 3000 cc. of whole blood and his circulatory condition had improved greatly. An emergency x-ray examination of the stomach and duodenum revealed absence of esophageal varices but showed a small duodenal defect. A subtotal gastrectomy was performed about 16 hours after admission. A posterior penetrating duodenal ulcer was found, and the findings indicated that perforation into the pancreas had taken place previously. The dissection was extremely difficult, and very little of the duodenum remained for closure. A Graham type of closure was performed, and two large drains were used. Care was taken so that neither of the drains would be in contact with the suture line. An end-to-side antecolic gastrojejunostomy was then completed. The bed of the ulcer in the pancreas continued to ooze blood, which oozing finally was controlled by fixing portions of the omentum and of the mesocolon to this bed. The immediate postoperative course was excellent. The patient was permitted out of bed within 48 hours, allowed small amount of fluids by mouth within 72 hours, and 4 days after surgery a progressive ulcer diet was begun. On the morning of the sixth postoperative day, during changing of dressings, an estimated 1700 ml. of bile and watery secretion was noticed draining from the stab wound about the drains. Serum electrolytes determinations were made immediately, and the levels were found to be as follows: potassium 4.0 mEq., chlorides 96.0 mEq., sodium 143.0 mEq., CO_2-combining power 21.6 mEq. Because of our previous experience, propantheline bromide was then administered intramuscularly on a schedule of 15 mg. every four hours day and night. Oral feedings were continued. Within a few hours after the administration of the first dose of propantheline bromide, the amount of drainage had lessened considerably and it was possible to allow the patient out of bed with only minimal dressings on the stab wound. Within 48 hours from the onset of the drainage its amount was reduced to about 500 ml. every 24 hours, and within three days from the onset the drainage was but 100 ml. daily. On the fifth day after the establishment of the fistula the drains were shortened, and on the seventh day they were completely removed. While it was assumed that fluid oral intake was satisfactory, it was conceded that protein intake by mouth was very poor. This was tentatively corrected by the intravenous administration of purified serum albumin in a 5% concentration at the rate of 100 ml. daily on alternate days. Plasma electrolyte determinations were not repeated, although an accurate check of intake and output of fluids was kept. The urinary output was normal throughout. On removal of the last drain the propantheline bromide was discontinued, and there was a discharge of pancreatic and biliary secretion estimated at about 1000 ml. for the first 12 hours. Intramuscular propantheline bromide therapy was administered, on the same dosage schedule, and within 48 hours the drainage completely stopped. On the 20th postoperative day, 14 days after the appearance of the fistula, this patient was sent home, with the drainage wound slowly healing and without any noticeable discharge. Oral propantheline bromide was given him for an additional four weeks, after which the drug was slowly withdrawn. A nine-month follow-up examination has

revealed complete and satisfactory healing of the fistula.

Summary

The use of intramuscular propantheline bromide in two cases of pancreaticoduodenal fistula, postgastrectomy, is described. We feel that this drug is of value because it markedly diminishes, or abolishes, pancreaticoduodenal secretions; hence it facilitates the management of a satisfactory electrolyte and fluid balance. An early closure of the fistula has been observed in the two cases.

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Ambulatory Treatment of Varicose Leg Ulcers with Fresh Placental Dressings

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Introduction

Permanent eradication of varicose leg ulcers through preventive measures or by surgical correction [1] of the underlying pathology is the ultimate therapeutic goal in this problem. Unfortunately, at present, the final answer does not exist, as evidenced by the number of patients in our clinic and elsewhere with the chronic leg-ulcer problem. Until a permanent, totally successful method of treatment is realized, the dressing of chronic leg ulcers will necessarily continue. The time required, the practicability, and the expense to obliterate these leg ulcers are of considerable importance to the patient and the physician.

The use of fresh human placenta in the management of war wounds was recently suggested by Chippaux.[2] This group, with the French Expeditionary Forces, applied various types of placental grafts to compound fractures and other open necrotic infected wounds. They frequently found contaminated wounds were rendered sterile, necrotic processes were arrested, and open wounds of soft parts and bone were filled as a result of the integration of the placenta with underlying tissue. They believed these grafts promoted granulation and epithelization. Ojetti [3] and Kubisty [4] claim good results with local application of placenta in the management of various chronic leg ulcers.

Local and systemic therapies for the obliteration of varicose leg ulcers in the recent literature were reviewed and include the following: penicillin and anesthetic injection of the ulcer,[5] muscle adenylic acid intramuscularly with local dry dressing, and elastic bandage;[6] absorbable gelatin sponge;[7] nitrofurazone (Furacin) soluble dressing;[8] enzymatic debridement;[9] respiratory enzymes intramuscularly;[10] resin, petrolatum (Vaseline) gauze, gauze bandage, and elastic adhesive bandage;[11] compression dressings;[12] local chlortetracycline (Aureomycin) ointment,[13] and bed rest.[14] Generally, the time necessary for the obliteration of the varicose leg ulcers was a matter of months, the per cent of successful results frequently low, and the various therapies complicated, often expensive or impractical.

Nineteen ambulatory patients with 30 leg ulcers were treated with placental dressings and observed from three to seven weeks at the Ohio State University Out Patient Clinic.

Preparation of Placenta

In an aseptic manner, as soon after delivery as possible, the membranes are stripped from the cotyledonous portion of the placenta and the former discarded. The cotyledonous portion is divided into 1 to 2 cm. cubes, and the blood and debris are removed with a sterile saline wash. These cubes are then placed in a sterile ointment jar in a loosely packed, one-layer arrangement, to which has been added 100 cc. of sterile normal saline, 1,000,000 units of aqueous crystalline penicillin, and 0.5 gm. of streptomycin. The covered ointment jar is placed in an ordinary refrigerator (35-40 F), and the placental cubes may be used several days to three weeks after preparation. This is essentially the same method of preparation as described by Chippaux.[2]

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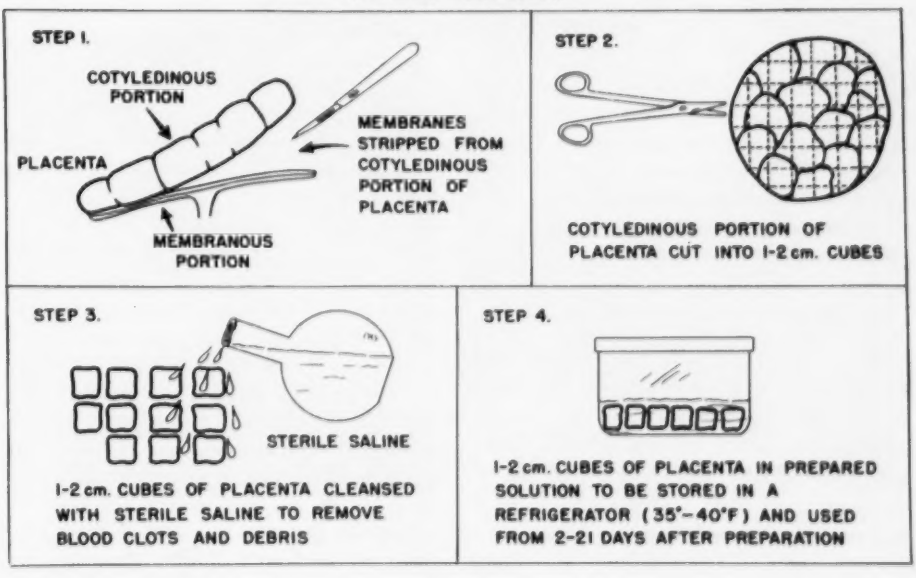
From the Department of Surgery and the Medical Center of The Ohio State University College of Medicine.

Placental Application to Ulcers and Follow-Up Care

The leg and ulcerated area is cleansed several times with a skin detergent (Phisoderm) and benzalkonium (Zephiran) chloride, the ulcer crater is gently mechanically debrided, and finally the ulcer area is irrigated with sterile saline. The cubes of placenta are partially dried between layers of gauze and cut in such a manner that the ulcer crater is filled with placental tissue one layer thick. Sterile dry gauze flats are applied directly over the placental tissue, and an elastic bandage is wrapped from the toes to the knee. Adhesive tape is then placed around the elastic bandage especially over the ulcer area to insure minimal movement of the placental tissue on the ulcer crater. The patient is dismissed, and this dressing is left intact until the patient returns in one week. No further instructions are needed, and the patients are permitted to carry on their normal daily routine. Generally in one week, at the time of the first dressing change, a dry or slightly moist crust is present over the previously ulcerated area and the only treatment necessary is a careful daily dressing change by the patient. This is best accomplished at bedtime when the patient carefully removes the elastic bandage and the dry gauze flat and permits the placental covering to dry during the night; this prevents maceration and speeds permanent healing. On arising, a clean dry flat gauze is placed over the lesion and the elastic bandage is reapplied; no adhesive is necessary. When the placental crust is completely dry, hydrous wool fat (lanolin) may be gently applied to the crust and surrounding skin. Soon after the crust has dried, it disintegrates and leaves an epithelized surface. After the ulcer has been obliterated, the patients are instructed to continue the daily use of elastic bandages or stockings during their waking hours. In one-third of the varicose ulcers treated, a second application of placenta was necessary. This usually was indicated at the

STEPS IN THE PREPARATION OF FRESH HUMAN PLACENTA FOR USE IN THE TREATMENT OF VARICOSE LEG ULCERS

(ASEPTIC TECHNIQUE)


STEP 1.
COTYLEDINOUS PORTION
PLACENTA
MEMBRANES STRIPPED FROM COTYLEDINOUS PORTION OF PLACENTA
MEMBRANOUS PORTION
STEP 2.
COTYLEDINOUS PORTION OF PLACENTA CUT INTO 1-2 cm. CUBES
STEP 3.
STERILE SALINE
1-2 cm. CUBES OF PLACENTA CLEANSED WITH STERILE SALINE TO REMOVE BLOOD CLOTS AND DEBRIS
STEP 4.
1-2 cm. CUBES OF PLACENTA IN PREPARED SOLUTION TO BE STORED IN A REFRIGERATOR (35°-40°F) AND USED FROM 2-21 DAYS AFTER PREPARATION

STEPS IN THE APPLICATION OF FRESH HUMAN PLACENTA TO VARICOSE LEG ULCERS

STEP 1.
PREPARATION OF VARICOSE ULCER CRATER
1. GENTLE PHISODERM® AND ZEPHIREN® SCRUB OF LEG AND ULCER
2. GENTLE MECHANICAL DEBRIDMENT
3. IRRIGATION WITH STERILE SALINE
STEP 2.
APPLICATION OF PLACENTAL TISSUE TO ULCER CRATER
1-2 cm. CUBE OF PLACENTA
PLACENTA CUBE CUT TO DESIRED THICKNESS SO THAT ONE LAYER FILLS ULCER DEFECT FLUSH
SIZE OF ULCER WILL DETERMINE NUMBER OF PLACENTAL CUBES USED
STEP 3
SEVERAL STERILE GAUZE 4"x4" PADS PLACED OVER PLACENTAL DRESSING
STEP 4
ELASTIC BANDAGE WRAPPED FROM TOES TO KNEE AND REENFORCED WITH ADHESIVE STRIPS

NO RESTRICTION IN NORMAL DAY TO DAY AMBULATION IS REQUIRED
DRESSING IS CHANGED IN ONE WEEK

first dressing change one week after the original application. In general, these are the deeper ulcers, and the ulcer crater with its placental bed is prepared in a fashion similar to that originally described. The leg is then re-dressed as before, and the dressing is changed in one week.

Summary of Ulcers Treated

All patients during the placental dressing therapy were ambulatory without restriction in their daily routine. Twenty-two primarily varicose ulcers with and without other complications (old thrombophlebitis, lymphedema, arteriosclerosis, trauma, etc.) were treated and observed during a seven-week period. Sixteen of these ulcers were obliterated during this seven-week period; eight of these required four weeks or less for complete obliteration. Five after a period of seven weeks, while improved in varying degrees, had not been completely obliterated. One patient was lost to follow-up. Initially, pain was present in 50% of the ulcers; however, 48 to 72 hours after the application of placental dressings the patients were asymptomatic in most cases. Six ulcers from other causes, including arteriosclerosis, burns, and Buerger's disease, were treated and had generally a poor response. Some improvement of the lesions was noted and some of the symptoms subsided, but the result in general was poor.

Controls for this placental therapy consisted of the length of time necessary for

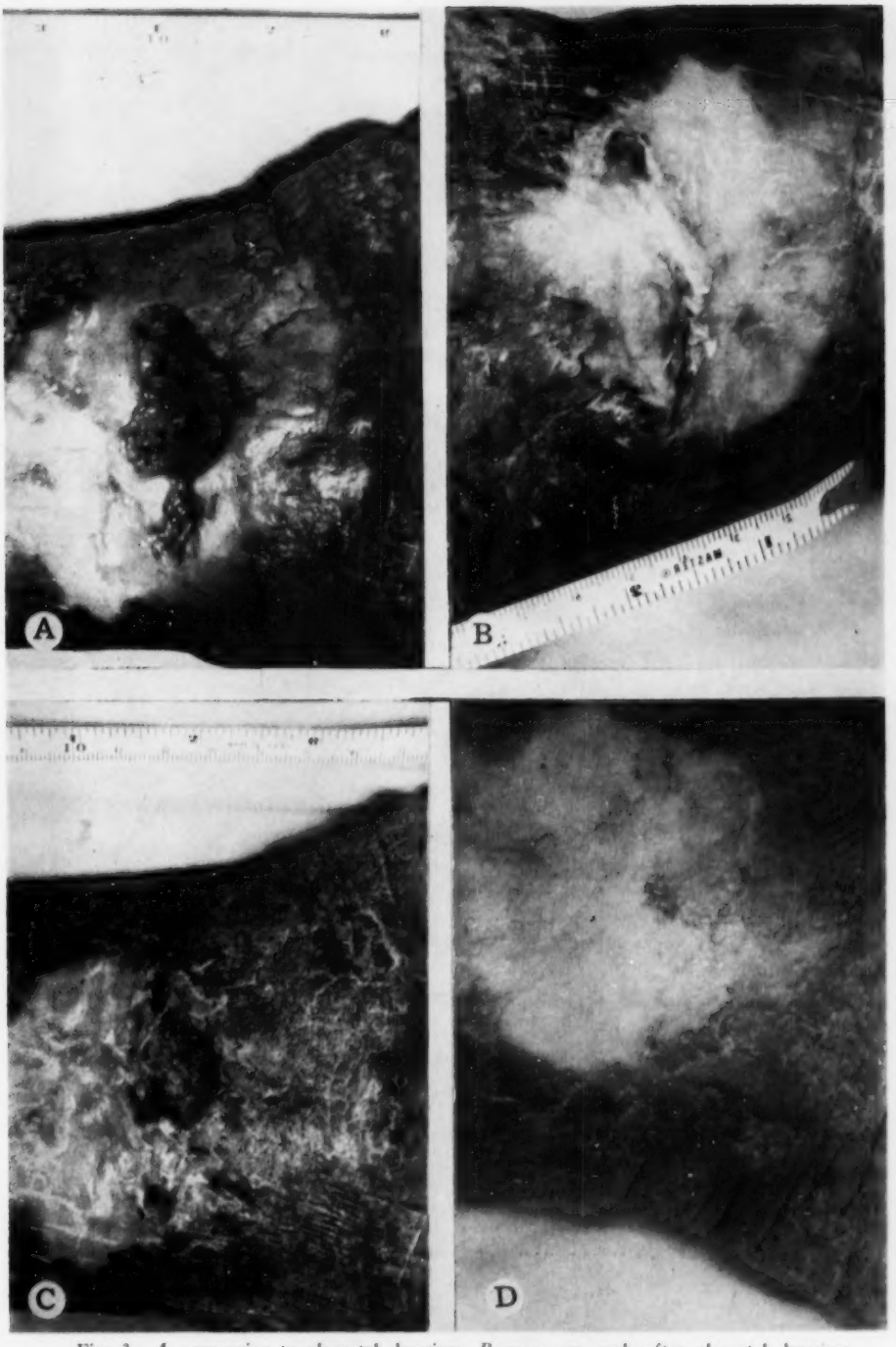


Fig. 3.—*A*, case prior to placental dressing. *B*, case one week after placental dressing, with a slightly moist crust covering ulcer crater. *C*, case two weeks after placental dressing with a dry crust covering ulcer crater. *D*, case five weeks after placental dressing with a disintegration of the crust and an epithelized surface.

obliteration of leg ulcers on the same patients with conventional treatment at the Ohio State University Out Patient Clinic. At least 80% of the patients in this series had been previously treated, and all required longer periods by weeks and months for obliteration of their ulcers by conventional means.

Typical Case

A 59-year-old Negro man had old thrombophlebitis, varicose veins, lymphedema, and diabetes mellitus with mild arteriosclerosis. Previous treatment during the past 12 years included a variety of local agents in general use and Unna boots. On reviewing this patient's clinic record, it was noted that the shortest previous obliteration time was six months. The ulcer at the time of the first placental dressing was 6×2 cm. in diameter and was located over the right medial malleolus. Pictures (Fig. 3, *A*, *B*, *C*, and *D*) were taken prior to placental dressings and at one, two, and five weeks.

Possible Mode of Action

Placental tissue by its very nature is concerned with cellular growth and proliferation. The cotyledonous or biologically functional part of the placenta is composed primarily of a fibrous stroma through which is dispersed a multitude of embryonic cells. Frequently, in the laboratory, various preparations of embryonic cells are utilized to stimulate tissue cultures. It would not seem unreasonable to suggest that these embryonic placental cells may have a stimulating effect on the slow-growing, unhealthy-appearing granulations present in varicose ulcer beds.

The placental cells contain readily measurable quantities of hormones which include adrenocorticotropic hormone and possibly certain corticoids, both of which are associated with a decrease in the fibrotic response in wounds. Numerous enzymes are present and most certainly include those involved in tissue respiration which have been utilized with some success in the treatment of leg ulcers. In addition, many vitamins have been identified in these placental cells with significant quantities of ascorbic acid. Immune bodies with their antibacterial properties are also present. Certain other basic chemical building blocks together with utilizable nutrients must be bound within these embryonic cells which may further have a favorable influence on cellular growth and proliferation.

The placental dressing would not seem to act as a graft per se, as the fate of homografts is well known. Instead, it would appear likely that the placental cell and its contents locally stimulate copious clean granulations in the prepared ulcer crater. The fibrotic placental matrix may well act as a lattice through and around which these healthy granulations may grow. At least early, these embryonic cells may provide nourishment to this granulating surface. It is well known that once a granulating surface becomes flush with the surrounding epidermis the migration of epithelium from the adjacent areas is hastened. The superficial placenta crust which forms in every way resembles an abrasion crust which certainly protects the new sensitive epithelium growing below.

The place of elastic compression bandages in the treatment of leg ulcers has been well established. The decrease in the superficial stasis and the increase in the deep circulation both have favorable effects on varicose ulcers. Ambulation, in addition, enhances the circulation and decreases stasis through the well-known mechanism of the peripheral pump.

Comment and Conclusions

Chronicity and poor to absent response to other local agents was present in the majority of cases used in this series. The healing time prior to placental application (with conventional forms of treatment) was a matter of months instead of several weeks as with placental dressings.

Placental dressings, like other local and systemic therapy, are directed at the rapid obliteration of varicose ulcers with minimal time and expense on the part of the physician and patient. In those who refuse surgery or those with poor surgical results, this method offers less discomfort and mor-

bidity with weeping, foul-smelling lesions. No thought of permanent cure by this method is entertained.

Summary

Placental dressings are proposed as an ambulatory therapy for varicose leg ulcers.

Various local and systemic therapies for varicose ulcers reported in the recent literature are noted.

Preparation and application of the placental dressings are discussed.

Nineteen ambulatory patients with 30 leg ulcers were treated.

Possible modes of action are suggested.

The Ohio State University Health Center.

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Squamous-Cell Carcinoma of the Pylorus with Diffuse Metaplastic Gastritis

Report of a Case

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The occurrence of squamous-cell carcinoma of the pyloric end of the stomach in association with diffuse squamous-cell metaplasia of the glandular gastric mucosa is rare. The coincidence of these two lesions has, to our knowledge, never been described in the literature, and because of the rarity of such a condition this case is being reported.

Report of a Case

A 54-year-old Negro man was admitted to the hospital on June 7, 1955, with a history and physical findings not unlike that of carcinoma of the stomach. For "five to six" years the patient had complained of food dyscrasias, often being able to relieve the "indigestion" with sodium bicarbonate (baking soda). Three to four months prior to admission, all foods began to be intolerable. Pain developed which was almost constant, and the patient began to lose weight constantly. He had lost from 30 to 40 lb. over the course of his illness. His physical examination revealed an emaciated Negro man with a palpable mass in the region of his pylorus.

Preoperative gastrointestinal x-ray studies revealed a large filling defect with partial obstruction of the lumen of the pylorus. The preoperative diagnosis of carcinoma of the stomach was made.

The patient was prepared for surgery and on June 8, 1955, a palliative Billroth I type of gastric resection was done. The lesion was a large tumor involving the entire pylorus and a portion of the antrum. Within the gastrohepatic ligament were several large lymph nodes which were thought to be invaded. Many nodes were removed, but, because the procedure was being done for palliation, no extensive lymph node resection was done. No lesions were seen within the liver. It was felt that the tumor probably extended to the line of excision.

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From the Department of Surgery, University of Tennessee, and the Department of Pathology, St. Joseph Hospital; Resident in Pathology, St. Joseph Hospital (Dr. Affolter).

Surgical Pathology.—The specimen consisted of a previously fixed sleeve of stomach measuring 12 by 7.5 by 5 cm. Small portions of fatty omentum were attached. The stomach was opened along the lesser curvature. The gastric lumen was markedly narrowed near the pyloric end. A large shallow ulcer was encountered on the greater curvature, beginning immediately above the pylorus. The ulcer measured approximately 6 cm. in length, 2 cm. in width, and 0.2 cm. in its greatest depth. The base of the ulcer was made up of grayish-white firm tumor tissue. The mucosa in the antral region showed a grayish, lusterless appearance, with flattened rugae. On cut section, the neoplasm was found to circumnavigate approximately two-thirds of the gastric wall at the proximal end and three-fourths of the circumference at the pyloric end of the specimen. The lesser curvature with the adjacent portions of the anterior and posterior walls of the stomach were grossly free of tumor. Along the greater curvature the neoplasm invaded the full thickness of the markedly thickened gastric wall, which measured up to 3.5 cm. in thickness. Proximally and distally, the neoplastic tissue extended to a point 0.5 cm. and 1.5 cm., respectively, from the line of excision. Seven firm lymph nodes, the largest measuring 1 cm. in diameter, were found.

Microscopic Examination.—Step sections were taken along the greater and lesser curvatures. The large ulcer on the greater curvature was covered by a layer of necrotic and hyalinized material containing numerous inflammatory cells. Beneath this necrotic zone there was a broad layer of loose, highly vascular, connective tissue containing large sheets and islands of neoplastic squamous cells. The tumor extended from the ulcer in all directions and invaded the entire gastric wall, including the serosa. Many of the large neoplastic islands showed central cavities filled with cell debris. Some of the squamous cells were arranged in

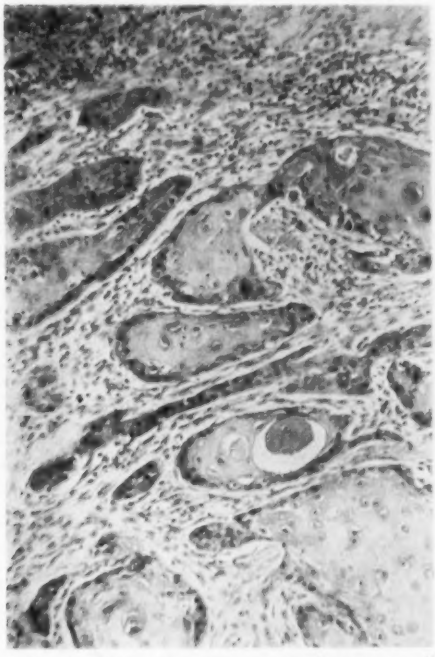

Fig. 1.—Nests of squamous epithelial tumor cells in the gastric submucosa. The neoplastic cells are arranged in whorls and show keratinization.

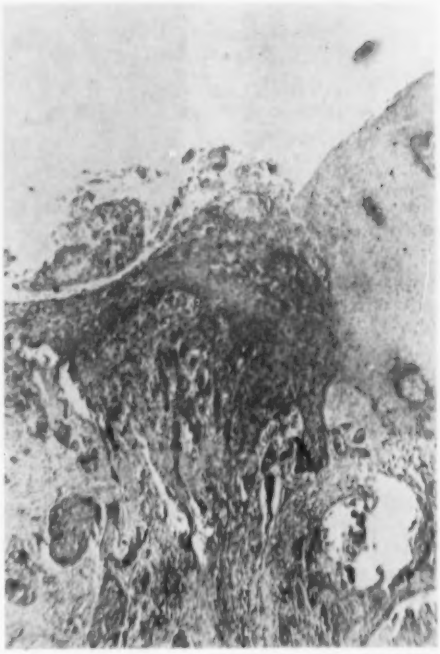

Fig. 2.—Section from greater curvature showing transition of metaplastic hyperplastic squamous epithelium on right into invasive squamous-cell carcinoma on left.

whorls and showed central keratinization (Fig. 1). The large, polygonal tumor cells revealed an acidophilic cytoplasm often containing flattened pycnotic nuclei. Single cell keratinization and cells with intercellular bridges were readily seen. Mitotic figures were common. The connective tissue stroma was of varying density and diffusely infiltrated by polymorphonuclear leukocytes, numerous eosinophils, and round cells. Tumor permeation of vascular and lymphatic channels could be demonstrated. There was no evidence of glandular formation. On the proximal circumference of the ulcer and extending from the margins of the ulcer up to the line of resection, the lining of the gastric mucosa consisted of stratified squamous epithelium which had replaced the glandular elements. There was marked fibrosis, with varying round-cell infiltration of the subepithelial tissue, the muscularis mucosae, and the submucosa. Toward the margins of the ulcerated area there was gradual thickening of the squamous epithelium, with progressive distortion of its architectural pattern, cellular pleomorphism, increase in number of mitotic figures, and, finally, transition into invasive squamous-cell carcinoma (Fig. 2) The gastric mucosa on the distal side of the ulcer was orderly and glandular and showed chronic inflammatory reaction. Along the lesser curvature the gastric glands and the columnar lining were almost completely replaced by stratified squamous epithelium which extended from the fundal end distally for approximately 3.5 cm. (Fig. 3). At this point there was transition into a markedly atrophic, chronically inflamed glandular mucosa. The stratified squamous epithelial lining was of slightly varying thickness, and there was, again, considerable fibrosis and round-cell infiltration of the subepithelial stroma and the hypertrophied muscularis mucosae. The areas of squamous metaplasia of glandular mucosa along the lesser curvature showed no evidence of invasiveness. Distally the atrophic glandular mucosa revealed gradual transition into the pyloric mucosa. Examination of the regional lymph nodes revealed metastases of pure squamous-cell carcinoma in five of seven nodes.

Postoperative Course.—The patient's immediate postoperative course was complicated by a rather severe pulmonary embolus, but the patient survived and was discharged from the hospital on July 2, 1955.

The patient failed to regain strength and shortly after discharge began to vomit after each feeding, although he was taking six to eight feedings

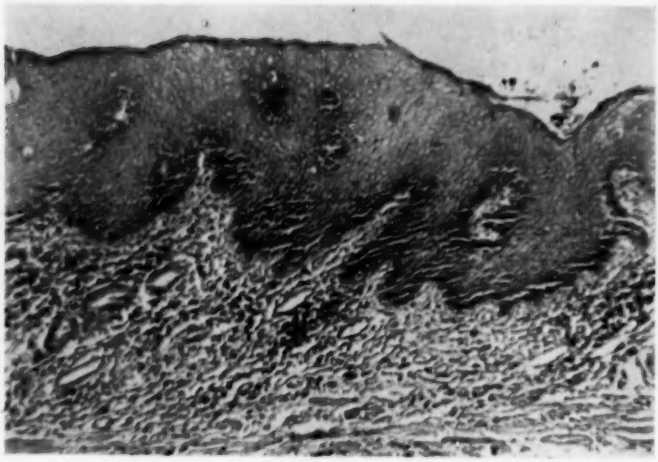

Fig. 3.—Section from lesser curvature showing almost complete replacement of the normal gastric mucosa by stratified squamous epithelium. Note the round-cell infiltration and the few remaining atrophic mucous glands in the subepithelial tissue.

a day. On Aug. 10, 1955, it was felt that the patient should be readmitted because of what was thought to be an obstruction probably due to extension of his disease. He was admitted to John Gaston Hospital, the Hospital of the University of Tennessee School of Medicine, and a preoperative gastrointestinal x-ray revealed almost complete obstruction of the stomach. He was prepared for surgery, and on Aug. 14, 1955, an exploratory operation was done. At surgery an obstruction of the anastomosis was found. The obstruction appeared to be due to scar tissue. The lymph nodes that were left behind at the previous surgery were now small, and nowhere could be found any evidence of residual disease. The previous anastomosis was resected, and a second Billroth I type of procedure was done.

Although the previous microscopic and gross examination revealed evidence of carcinoma near the section line, no tumor could be found in the second specimen after a thorough search. The microscopic examination revealed scar tissue with foreign-body reaction.

Following this surgery, the patient did unusually well. He regained his preoperative weight and returned to work. Five months after his second operation, difficulty in emptying the stomach began. This difficulty progressed in severity until he could retain no ingested food. He was readmitted to The John Gaston Hospital on March 14, 1956. X-ray studies then revealed a complete obstruction of his stomach outlet. Again, he was advised to have another exploration. This the patient refused, and he "signed out" of the hospital. He died on April 19, 1956, and we were unable to obtain a postmortem examination.

Comment

One of the first exhaustive and critical surveys of the literature pertaining to squamous-cell carcinomas of the stomach was by Wood [1] in 1943. He listed nine cases of pure epidermoid carcinoma of the pyloric region. In reviewing the subsequent literature, we found seven additional reports of such tumors.[2-7] From experimental and clinical evidence, Wood concluded that direct neoplastic stimulation of undifferentiated basal cells in the gastric mucosa was the essential factor in the histogenesis of squamous-cell tumors of the pyloric region of the stomach. Reich,[2] however, believed that the neoplasm might have been secondary to squamous metaplasia due to chronic atrophic and hypertrophic gastritis in the case reported by him, whereas Casanova-Diaz [5] cited Duran-Jorda, who described the existence of a a flat epithelial layer at the top of the gastric and intestinal mucosae. He felt that the epidermoid carcinomas and adenoacanthomas originated from this layer.

Diffuse squamous metaplasia of the gastric mucosa is extremely rare. Hermann [8] described the incidence of squamous metaplasia of the pyloric mucosa in the stomach of a 36-year-old woman who had suffered from two cicatricial gastric stenoses. He assumed that mechanical trauma was an important pathogenetic factor in this lesion.

Watson, Flint, and Stewart [9] reported a case of hyperplastic tuberculosis of the stomach causing an hourglass deformity with extensive squamous metaplasia of the upper loculus. They left the question open whether the metaplastic changes were secondary to the changed environment resulting from the midgastric obstruction or whether this was a downward extension of the squamous epithelium of the esophagus. Sailer [10] found diffuse squamous metaplasia comprising almost two-thirds of the lining surface of an unusually small stomach in a patient with prolonged cachexia and macrocytic anemia. There was no apparent cause for the gastric changes, and the author considered the possibility of a vitamin A deficiency. Strassman [11] observed a small area of metaplastic squamous epithelial lining on the greater curvature in a case of adenoacanthoma of the stomach. He believed that the squamous epithelium was derived from undifferentiated basal cells in the gastric mucosa which had undergone metaplasia after chronic inflammation of the stomach, and that these cells were the site of origin of the squamous component of the tumor.

The relationship between squamous metaplasia and squamous-cell carcinoma has been an issue in the past. Ewing [12] stated that squamous metaplasia affected the cells before the development of an epidermoid carcinoma in unusual locations, whereas Willis [13] believes that the theory of squamous-cell carcinoma arising from an epithelium in which metaplasia has already occurred is erroneous and that the change is a property of the tumor itself and unrelated to precancerous states of the tissue. A histogenetic theory, originally suggested by Fischer-Wasels,[14] which explains satisfactorily the problem of squamous metaplasia and of the development of malignant squamous-cell tumors from glandular epithelium, has been outlined by Dockerty.[15] It is based on the observation that destroyed or severely damaged glandular epithelium is replaced in kind by proliferation of basal or reserve cells normally present in the mucosa. Repeated destruction of these newly formed elements leads to hyperplasia of the reserve cells. If this is followed by further demands for replacement, a state of basal-cell anaplasia results, in which the ability to redifferentiate normally is lost. The products of such cells may be glandular, squamous, or mixed, and the resulting tissue, benign or malignant.

In our case, we had the unusual opportunity to observe chronic gastritis associated with diffuse squamous metaplasia and transition of the metaplastic epithelium into pure squamous-cell carcinoma which metastasized to the regional lymph nodes. In view of these findings, we assume that the metaplastic and neoplastic squamous cells originated from the same primitive cells. In accordance with the above-cited theory, we believe that under the stimulus of chronic inflammation a state of anaplasia of the basal cells occurred and that these cells subsequently gave rise to the metaplastic and neoplastic squamous elements.

Summary

A case of primary squamous-cell carcinoma of the pyloric end of the stomach associated with diffuse metaplastic gastritis is presented. The possible histogenesis is is outlined.

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Differential Hypothermia in Experimental Hepatic Surgery

Application of This Technique to a Problem in Clinical Surgery

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Introduction

"The whole problem in cases of resection of the liver has turned upon the question of the control of hemorrhage from the wound."[1] Oozing from the cut liver surface results in considerable blood loss and obscures the operative field, making identification and control of bleeding from major vessels difficult. Various techniques of mass hemostasis have been developed to cope with this problem; through-and-through mattress sutures, with or without compression plates,[1,2] cautery,[3] exteriorization and gradual removal of peripheral hepatic lesions.[4] Although success has been reported with these methods, they have the following disadvantages: (1) deliberate resection with definitive hemostasis and control of biliary leakage is not permitted; (2) devitalized tissue is left within the abdomen, and (3) the techniques are suitable only for small peripheral lesions.

Preliminary isolation and ligation of vessels supplying and draining the right or left lobe before hepatic lobectomy has been described by French workers.[5,6] Successful results using this technique have been obtained by Pack[7] and Brunschwig.[8] Such procedures, however, necessitate removal of the entire right or left lobe. Collateral circulation between the two major lobes is frequently extensive, and the operative field is not always dry.[7] To assure a dry field the surgeon must resect only within the devitalized area, leaving a zone of devascularized tissue.

Temporary interruption of hepatic blood flow would appear to be a desirable adjunct to hepatic surgery. This would permit delicate resection of any segment of the liver. Individual ligation of vessels and bile ducts could be performed at the resection edge, thus leaving a minimum of devitalized tissue within the peritoneal cavity.

Because of the location of the liver with its double afferent blood supply, one must consider the liver, spleen, and gastrointestinal tract as an integral vascular unit. Interruption of hepatic afferent blood flow results in hepatic ischemia and, of necessity, either ischemia or congestion of the portal bed, depending on the site of occlusion.

The effects of such occlusion in the dog have been well described. Raffucci and Wangensteen have found 20 minutes to be

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This article, in addition to giving a summary of the previous work, describes the modifications of the technique which we are currently employing. That is, the site of arterial vascular occlusion has been changed from the abdominal aorta to the hepatic artery in the porta hepatis. The employment of a simple polyvinal shunt to decompress the portal bed in such animals is described. We feel that this variation in the technique is a most important one. Finally, a description of the first clinical case in which this technique was utilized is included in this second article and was not present in the report of the initial experimental work.

The opinions or assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the view of the Navy Department or the Naval Service at large.

the maximum safe period for occlusion of the hepatic artery and portal vein in the porta hepatis.[9,10] The procedure was almost invariably lethal when prolonged for periods of 30 to 60 minutes. The livers of their dogs showed histologic evidence of necrosis. The importance of portal congestion in this situation has been illustrated by Drapanas et al., who found that if an Eck fistula were produced as a preliminary procedure, dogs would tolerate 75 minutes of hepatic anoxia.[11] State and Lichtenstein, on the other hand, reported that death occurred within 20 minutes following restoration of hepatic arterial flow even if portal pooling was prevented by means of a portacaval cannula when afferent hepatic blood supply had been interrupted for 1 hour.[12] These authors also reported histological evidence of hepatic necrosis in their animals.

Burch,[13] Edwards,[14] and we[15] have reported that death usually follows 60 minutes of occlusion of the aorta above the celiac axis. It appears that interruption of circulation to the liver for one hour, either proximal or distal to the intestinal tract, results in a high mortality with evidence of liver necrosis.

Very little information is available on the effect of hepatic ischemia in man. Permanent ligation of the hepatic artery distal to the gastroduodenal artery in patients without portal hypertension is generally lethal.[16] Gradual occlusion of this vessel over a period of days or weeks may, however, be tolerated.[17]

Wangensteen has temporarily occluded the hepatic artery and portal vein in three patients. One patient survived 33 minutes of occlusion. A second patient survived 20 minutes of occlusion but was oliguric for days. A third patient died with persistent hypotension following a total of 27 minutes of occlusion, even though this period of vascular occlusion was interrupted with a 20-minute period of restored blood flow.[18,19] Brunschwig has had two deaths following 30- to 45-minute interruptions of the hepatic circulation. One of these patients died of cardiac arrest and the other of persistent hypotension despite transfusions.[20]

The reduction of metabolism afforded by general hypothermia has been shown to prolong "safe" periods of circulatory interruption to vital structures. Bernhard et al.,[21] working with dogs, and Shumway and Lewis,[22] with dogs and man, have demonstrated the feasibility of partial hepatic resection utilizing afferent vascular occlusion and general hypothermia to protect against the lethal effects of such occlusion. Hepatic circulation was occluded from 33 to 45 minutes in the four human cases reported.

The following experiments were performed in an attempt to devise a more widely applicable technique for partial hepatectomy.

Methods and Results

Male mongrel dogs, unselected as to age and weight, were used in these studies. All operations were performed through a midline abdominal incision with a sternum-splitting extension where necessary for exposure. Intravenous pentobarbital sodium was used for anesthesia. No antibiotics or special preparation were given preoperatively or, except when specifically stated, postoperatively.

All surviving animals were followed for a minimum of three weeks. Sulfobromophthalein (Bromsulphalein) retention tests (5 mg. of dye per kilogram with blood analysis 45 minutes after dye administration) were usually performed one week after operation and again before killing.

In 2 groups of 10 dogs each, the aorta above the celiac axis and the portal vein in the porta hepatis were occluded for 60 minutes at normal temperature. The first group received no special postoperative supportive therapy. After surgery, the second group was given 1000 ml. of isotonic saline intravenously, 0.2 gm. chlortetracycline intravenously, and 1,500,000 units of aqueous penicillin and 1.0 gm. of dihydrostreptomycin sulfate intramuscularly. All surviving animals in the second group were also given 0.5 gm. of chlortetracycline by mouth each day for five days. One of the ten animals in the first group and four of the ten animals in the second group survived

and appeared healthy when killed three weeks postoperatively. The dogs that died showed necrotic changes in the liver and intestinal mucosa.

Direct intraperitoneal cooling was performed on a third group of 10 dogs. The peritoneal cavity was filled by pouring sterile saline at a temperature of 2 to 10 C directly into the abdomen through the laparotomy incision. The viscera were then gently agitated, and the saline was aspirated and discarded. A total of 8 to 10 liters was used in this manner. Within 10 to 15 minutes after cooling began, the intestinal temperature fell to a level between 17 and 20 C and that of the liver fell to between 20 and 24 C (Fig. 1). One hour after the active cooling period was completed the midesophageal temperature was 30 to 32 C. At this time, rewarming was carried out with sterile saline at 40 to 45 C. The abdomen was then closed without drainage. All 10 animals survived and were healthy when killed. The abdominal viscera were normal to gross and microscopic examination.

Intraperitoneal cooling as described above was next performed on two groups of dogs prior to occluding the abdominal aorta above the celiac axis and the portal vein in the porta hepatis for one hour. One group of 10 dogs received no special postoperative supportive therapy. A second group of 10 dogs received the same postoperative regimen previously outlined for the normothermic control animals. All animals recovered promptly from anesthesia. Seven of the ten dogs that did not receive antibiotics died of infectious complications 3 to 15 days postoperatively. None of the 10 animals receiving supportive therapy died. All were healthy and had normal appearing viscera when killed three weeks later. Histologically, the liver, intestines, and kidneys were normal. Histochemical techniques demonstrated normal glycogen and fat content in the livers of those animals that had been cooled. This was in marked contrast to the decreased glycogen and increased fat deposits seen in the few normothermic control animals that survived.

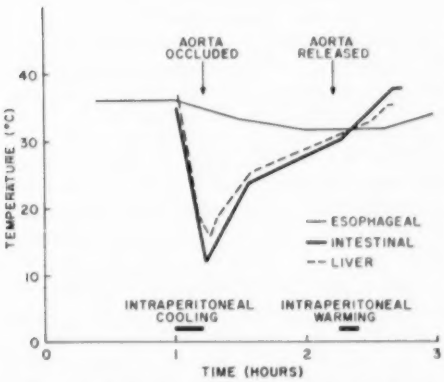

Fig. 1.—Temperature changes of midesophagus, intestine, and liver during cooling, vascular occlusion, and warming.

The success of preliminary intraperitoneal cooling and postoperative antibiotic and intravenous fluid therapy in preventing the gastrointestinal hemorrhage, liver damage, and death associated with 60 minutes of occlusion of the aorta above the celiac axis was encouraging.

Next, partial hepatic resections were performed in two groups of dogs during the period of circulatory interruption. In the first group, of 30 animals, intraperitoneal cooling was performed prior to occlusion of the aorta above the celiac axis and the portal vein in the porta hepatis. From 15% to 90% of the liver was removed, without any attempt to clamp intrahepatic vessels and bile ducts before transection. The open vessels were sutured and ligated with fine nonabsorbable surgical (silk) sutures. Aortic occlusion was maintained for 60 minutes in 26 of the animals, and in the other 4 occlusion was terminated as soon as hemostasis had been obtained. No oozing occured from the cut surface of the liver upon release of the clamps. The absence of oozing made identification and definitive control of the large vessels easy. Eight of the thirty animals died of complications which appeared unrelated to the acute effects of circulatory interruption.

Occlusion of the aorta above the celiac axis in man would not be desirable nor could it be easily accomplished through a right-sided incision. Therefore, a modification of the technique was devised for human use. Ten animals underwent intraperitoneal cooling and occlusion of the hepatic artery and portal vein in the porta hepatis. To prevent portal bed pooling a small siliconed polyvinyl shunt (3.5 mm. internal diameter) was employed between the splenic vein and the femoral vein. Occlusion of the vessels in the porta hepatis was maintained for one hour, during which time 40% to 80% of the liver was removed. These animals all did well, with no mortality.

No cardiac complications or wound edge bleeding was seen in any of the 66 animals that underwent differential intraperitoneal hypothermia.

The feasibility and ease of such resections having been demonstrated in dogs, the technique was employed in one clinical case.

Report of a Case

The patient was a 14-year-old boy who came to this country from Greece 11 months previously. One month prior to admission to the Massachusetts General Hospital he noticed a large asymptomatic abdominal mass. On physical examination this was seen to move with respiration and was apparently attached to the liver. X-ray studies demonstrated a 14.5 cm. in diameter calcified cyst in the anterior portion of the right lobe which was consistent with the diagnosis of Echinococcus cyst.

He was transferred to the surgical services of the hospital, and on April 27, 1956, an exploratory laparotomy was performed by one of us (W. V. M.) through a right thoracoabdominal incision. A large tense thin-walled cyst was found overlying the vessels and bile ducts in the porta hepatis. The ligamentous attachments of the right lobe were taken down, and the structures of the gastrohepatic ligament were isolated. A siliconed polyvinyl shunt was placed between a branch of the middle colic vein and a left antecubital vein (Fig. 2). The peritoneal cavity was filled by pouring sterile saline at a temperature of 6 C directly into the abdominal cavity. After several minutes the saline was aspirated and the peritoneal cavity was again filled. Fourteen liters of saline were employed in this manner. Thirteen minutes after the first introduction of the saline, the hepatic artery was occluded. Two minutes later the portal vein was clamped and the shunt was opened. The cyst was excised intact with a margin of normal liver tissue. The hepatic artery was released 53 minutes after occlusion and the portal vein 9 minutes later. Twenty minutes after the hepatic circulation had been interrupted, the central liver temperature was 28 C. Midesophageal temperature fell only to 33.5 C, and rewarming was not deemed necessary. The anesthesia, differential hypothermia, and partial right hepatic lobectomy were apparently well tolerated, and the patient did well during the first week following operation. Pathological examination of the resected lesion confirmed the diagnosis of Echinococcus cyst. A sudden overwhelming staphylococcal septicemia then developed, with extensive bilateral pneumonia. A polyethylene catheter placed in one of the veins of the right upper arm for the purpose of administering intravenous fluids was suspected of being the source of the septicemia. The catheter was removed, and the cephalic vein was ligated. Death occurred on the 11th postoperative day. At postmortem examination a purulent thrombophlebitis of the right axillary vein was found. This was obviously the source of the septicemia and the multiple purulent foci found in both lungs. A wedge-shaped area of infarction was found in the remaining tissue of the right lobe of the liver. This was attributable to surgical interruption of the hepatic arterial supply to that area. No necrosis in the liver tissue to which the arterial supply was intact was observed.

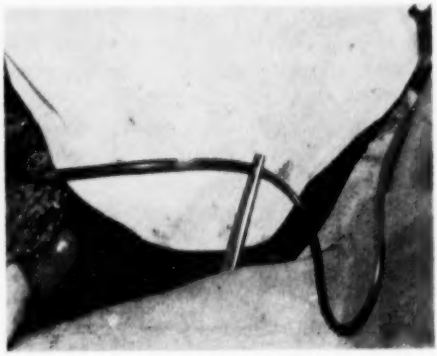

Fig. 2.—Polyvinyl middle colic-brachial venous shunt.

Despite the clinical failure in this case, the technique of differential hypothermia was successful, and no one concerned with the management of the patient felt that the unfortunate outcome was in any way attributable to the hypothermia.

The striking features of the operation were the dry field and the ease with which intrahepatic

Fig. 3.—Resection edge of liver; note absence of oozing.

structures could be identified (Fig. 3). Intraperitoneal cooling was simple and effective and did not predispose to shock.

Comment

The effectiveness of intraperitoneal cooling was demonstrated by the striking differences in mortality and histological apperance of the viscera of normothermic and cooled animals subjected to 60 minutes of occlusion of the aorta above the celiac axis and portal vein in the porta hepatis. The magnitude of the safety factor afforded by the cooling period was demonstrated by additional experiments in which 9 out of 15 animals survived 120 minutes of occlusion.[23]

A small temporary portal-systemic shunt adequately reduced portal bed pressure and permitted interruption of hepatic circulation in the porta hepatis during liver resection. The absence of valves in the portal system allows retrograde flow through a middle colic-antecubital venous shunt. Establishment and removal of a peripherally placed shunt appears preferable to anastomosis and subsequent venorrhaphy required with a portacaval shunt.

Differential intraperitoneal cooling offers numerous advantages over general hypothermia in prolonging safe periods of hepatic circulatory interruption. Lesions discovered at laparotomy may be resected without necessity of wound closure and reoperation under general hypothermia at a later date. Even when hepatic lesions are suspected, their extent and resectability often cannot be accurately determined preoperatively. The technique employing differential hypothermia permits the surgeon to evaluate resectability of hepatic lesions without committing the patient to general hypothermia or a staged operation.

The minimal degree of general hypothermia should reduce the incidence of cardiac complications and postoperative wound bleeding seen with general hypothermia. The simplicity, effectiveness, and apparent safety of intraperitoneal cooling would permit use of this technique in smaller hospitals as well as large medical centers.

Summary and Conclusions

Differential intraperitoneal cooling with cold sterile saline followed by postoperative antibiotic and intravenous fluid therapy was effective in preventing the gastrointestinal hemorrhage, liver damage, and death seen in normothermic control animals when the aorta was occluded above the celiac axis for one hour.

Extensive liver resections were performed following intraperitoneal cooling. These were accomplished during the period of occlusion of the afferent hepatic vasculature obtained by occluding the aorta above the celiac axis and the portal vein in the porta hepatis.

Similar resections were carried out with hepatic afferent occlusion in the porta hepatis. A peripherally placed shunt was employed to decompress the portal bed in these animals.

A technique employing differential hypothermia and occlusion of the hepatic artery and portal vein in the porta hepatis, with a middle colic to antecubital venous shunt, has been used in one human case. This technique appears to offer significant advantages over previously described techniques for partial hepatectomy.

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Duodenocolic Fistula Due to Carcinoma of the Hepatic Flexure

Report of a Case with a Discussion of the Surgical Problems Encountered

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The occurrence of a fistula between the duodenum and the proximal transverse colon is relatively rare, although these two structures commonly lie in intimate relationship to each other. It is not uncommon for tumors of the right colon and proximal transverse colon to involve the duodenum by contiguity, but the bowel symptoms usually lead to diagnosis and operation before a carcinomatous fistula develops between the colon and the duodenum. We have never seen a duodenocolic fistula caused by peptic ulcer disease.

The addition of a duodenocolic fistula to the problem of treatment of carcinoma of the colon is indeed a major handicap. The fistula adds profound disturbances in electrolyte, fluid, and protein (nutritional) balance which are difficult, if not impossible, to correct as long as the fistula exists. To operate without their correction is to court almost certain disaster. These problems and a method of their solution are presented because they may be of interest to others confronted with a similar situation.

Report of a Case

A 67-year-old white farmer was admitted to the Polyclinic Hospital at Harrisburg with a history of bouts of diarrhea for six months. These attacks consisted of watery bowel movements for two to three days, after which his bowel habit would return to normal. About a week prior to admission he noted an episode of sharp, severe, transient right flank pain which came on without apparent cause. Three days before admission he developed rather sudden severe diarrhea consisting of watery stools every 20 to 30 minutes throughout a 24-hour period. Vomiting began the day before admission, associated with a severe burning in the epigastrium. He believed that the vomiting and diarrhea were brought on by eating.

On physical examination there were no significant findings except flecks of blood noted in the bowel on proctoscopic examination. Stool test showed 4+ blood, and the BUN, which on admission was 60 mg. per 100 cc., gradually came down to 17 mg. per 100 cc.

The significant findings appeared on x-ray examination of the gastrointestinal tract. A barium enema demonstrated a fistula between the proximal transverse colon and the duodenum. Barium appeared in both the stomach

Fig. 1.— Duodenocolic fistula. Arrow points to fistulous tract within a carcinoma of the hepatic flexure extending to the lumen of the duodenum.

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Hospital of the Graduate School of Medicine of the University of Pennsylvania.

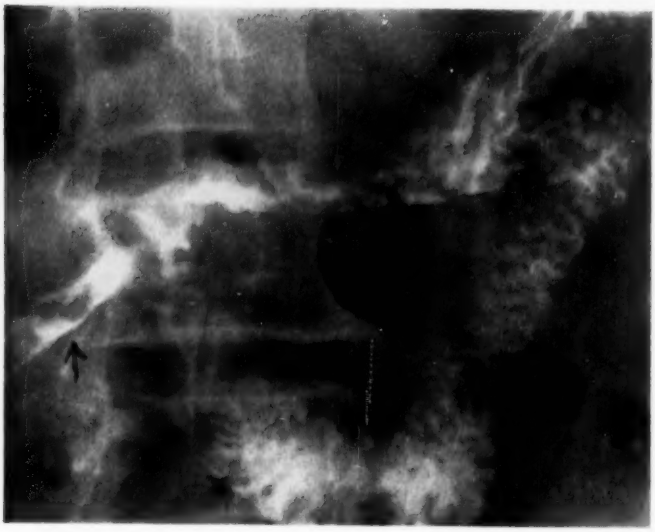

Fig. 2. — Position of fistulous tract showing extension from the lateral duodenal wall.

and the duodenum (Fig. 1). An upper gastrointestinal x-ray study showed the fistulous tract to extend from the second portion of the duodenum to the region of the hepatic flexure of the colon. The patient was transferred to the Graduate Hospital in Philadelphia.

After about two weeks' hospitalization his vomiting was continuing and was by this time definitely fecal in character. He had four to six watery bowel movements daily and showed evidence of dehydration. The results of his laboratory studies were as follows: Hemoglobin, 11 gm.; CO_2, 20 vol. %; chloride, 96 mEq./L.; potassium, 4.1. mEq./L.; sodium, 130 mEq./L.; total protein, 4.8 gm. per 100 cc.; (albumin, 2.9 gm. and globulin, 1.9 gm.); gastric analysis peak: total acid, 94 units, free acid, 60 units.

Over a period of four days he was given 1000 cc. of blood and 200 cc. of concentrated human serum albumin as well as intravenous fluids as indicated by the state of dehydration and electrolyte deficit. This elevated his hemoglobin to 12.1 gm., and his protein to 5.8 gm. (3.8 gm. albumin and 2 gm. globulin) and at the same time brought his electrolytes to within the normal range.

On the fifth day after admission to the Graduate Hospital his abdomen was explored through a midline incision. A large carcinomatous mass was found involving the hepatic flexure and proximal transverse colon. It was fixed to the retroperitoneal structures, but there were no palpable lymphatic or hepatic metastases. The abdominal contents were edematous and quite friable, and so a conservative procedure was decided upon. The ileum and its mesentery were divided about 12 in. from the ileocecal valve; the distal cut end was inverted and dropped back into the abdomen. The end of the proximal ileum was anastomosed to the side of the transverse colon to the left of the midline.

The patient made an excellent recovery after the procedure. His wound healed well, his vomiting stopped, and he was eating a soft diet by his fifth postoperative day. The diarrhea continued, however, as before, a barium meal study again showed the fistula through which a large part of the ingested barium passed directly from the second part of the duodenum into the colon. A well-functioning ileotransverse colostomy was demonstrated.

Maintaining the hemoglobin and protein levels with further transfusions and concentrated human serum albumin infusions, with fluid and electrolyte supplements, the patient was again operated upon, 14 days after the first procedure. The abdomen was opened through a transverse incision on the right side. The transverse colon was divided just proximal to the ileotransverse colostomy and the distal cut end closed. The right colon and terminal ileum were then mobilized, freeing edematous fixation of the tumor to the fatty capsule of the right kidney. The tumor was eventually freed from all sides and the blood supply controlled, until it was attached only to the duodenum at the fistulous tract. In mobilizing the duodenum the fistula was opened, and so it seemed best to complete the separation of the duodenum and bowel. When the main tumor mass had

Fig. 3.—Note filling of right colon with barium after a barium meal.

been removed, it appeared that the carcinomatous extension to the duodenum was in only a narrow ring around the fistulous opening. Plans which had been made for doing a radical duodenectomy were abandoned when it was found that the area of duodenum about the fistulous opening could be excised, leaving microscopically normal duodenum. Further mobilization of the duodenum permitted closure of the duodenal defect without tension. The abdomen was closed without drainage. The patient made an uneventful recovery and left the hospital on his 13th postoperative day; he was on a full diet and was having one or two bowel movements daily.

Comment

The duodenocolic fistula which was shown by x-ray to transmit intestinal contents in both directions presented a pathophysiologic picture similar to that seen in gastrojejunocolic fistula. It was immediately apparent that the risk of operation was grave unless the protein and electrolyte deficits and the marked dehydration could be corrected. It was also apparent that only temporary correction could be expected from replacement (blood, serum albumin, intravenous fluids) as long as the fistulous tract was present. The first conclusion, therefore, was to avoid any long period of preoperative preparation but to correct the disturbed physiology as well and as rapidly as possible and then operate.

The second consideration had to do with the type of operation to be performed. It seemed apparent from the first that an attempt at a radical resection involving a right colectomy and duodenectomy was more than should be carried out as a primary procedure. More conservative procedures with the purpose of reducing the disturbing effect of the fistula were considered. Diversion of the gastrointestinal contents from the duodenum was suggested. The duodenum was to be divided and turned in distal to the pylorus and continuity of the gastrointestinal tract to be reestablished by a Roux-en-Y type anastomosis. This operation, although diverting intestinal flow away from the duodenal fistula, was not seriously considered because it could be technically impossible to free the duodenum

Fig. 4.—Barium meal study after first operation. Five minutes after barium meal, note duodenocolic fistula indicated by filling of right colon and hepatic flexure.

and because it might interfere with a secondary radical resection.

Recognizing the similarity of the problems presented by this fistula and those of gastrojejunocolic fistulae, methods of fecal diversion used as a first stage in the operation for the latter fistulae were recalled to mind. Pfeiffer and Kent [1] suggested an ascending colostomy to divert the fecal stream from the area of the fistula. Marshall [2] described an ileodescending colostomy as a first stage to by-pass the fistula. Experience has shown that both of these procedures produced rapid improvement in the nutritional state of the patient so that a subsequent radical operation upon the gastrojejunocolic fistula could be carried out with a reasonable risk.

In the case under consideration, a colostomy proximal to the tumor seemed out of the question; ileostomy was possible but not desirable. Ileotransverse colostomy seemed reasonable to divert the intestinal flow from the area of fistula by making the ileum empty into the transverse colon distal to the fistula and tumor. This procedure would also be a stage of a subsequent resection.

At the first laparotomy, the latter operation was carried out with some question of success because of the edema and friability of the tissues. The outcome was good. The vomiting, due to regurgitation of fecal material from the colon into the stomach, stopped. As might be expected, the diarrhea due in part at least to the passage of duodenal contents into the colon persisted. It was possible to improve the patient's general nutritional state in preparation for a direct attack upon the fistula and tumor.

It was recognized that a curative operation was almost surely out of the question, but there was the slight chance that a curative procedure might be performed, since no liver metastases were demonstrated at the first operation. The operation of ileotransverse colostomy was looked upon as only a first-stage procedure in preparation for a resection of the tumor and fistula, the only operation that offered any hope of cure or even of palliation. The operative risk was recognized as grave but seemed justified, since no other procedure offered any hope of benefit.

There was considerable discussion as to how to handle the extension of tumor into and the anticipated defect in the duodenal wall. The fistula opened in the duodenal wall about opposite to the location of the ampulla. A Whipple type of duodenal resection was considered, or it was suggested that a disc of duodenal wall containing the ampulla might be saved and sutured into the jejunal wall used to re-form intestinal continuity after resection of the duodenum.

One of us has had experience with several cases of carcinoma of the right colon and hepatic flexure in which the tumor extended by contiguity to the duodenum. It was possible to resect a wedge of duodenum adherent to the tumor with the main tumor mass. The remaining defect in the duodenum could be closed by suture after mobilization of the duodenum. Microscopic study of the duodenum attached to the tumor showed only superficial local invasion of cancer cells. It seemed possible that such a conservative solution might work out in this case, and this proved to be true. It was recognized that under different circumstances a more radical operation might be desirable, but when the tumor was being freed it appeared that there were many areas of retroperitoneal tissue left behind which probably contained tumor. Since this was then a palliative operation, and since local excision of the tumor in the duodenal wall around the fistulous opening seemed feasible, consideration of a more radical procedure was abandoned. The rather large defect of the right anterolateral duodenal wall could be closed by suture after adequate mobilization of the duodenum. The suture line was covered over with a tongue of omentum.

No drainage was used, in spite of evident fecal contamination, because we believed that the formation of the fistula and the

previous operation had "vaccinated" this area. The antibiotics used in preparation of the bowel had reduced the probability of an active infection, and because we believe that the body tissues can take care of contamination, especially if they have been vaccinated, if the contamination is not continuing. The fact that the postoperative recovery was devoid of any suggestion of infection, of either wound or retroperitoneal area, perhaps justifies our belief in this regard.

Summary

A case of duodenocolic fistula due to carcinoma of the hepatic flexure of the colon is reported. Such a fistula adds many problems of nutritional, electrolyte, and fluid balance. The similarity of these changes to those found in gastrojejunocolic fistula is pointed out. The advantage of intensive replacement therapy, of operation without prolonged attempts at preparation, and of staged procedures is emphasized.

In the case reported the patient made a good recovery after a primary ileotransverse colostomy, with secondary right colon resection and repair of the duodenal defect.

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Restitution of Continence in Spina Bifida

The Tethered Cord Syndrome

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Persons born with any of the types of the congenital anomaly of spina bifida can present urological problems similar to those seen in paraplegics, where the etiology may be tumor, trauma, or infection. Although many varieties of spina bifida exist, it is in the more extensive types, meningomyelocele and myelocele, that the neurologic deficit seriously compromise vesical and rectal continence. Despite orthopedic and neurosurgical successes in the early repair of such deformities and in rehabilitative therapy, little if any advance has been noted consequent to therapeutic attacks upon urinary and fecal incontinence. There has been additionally, in many instances, a gradual deterioration of the upper urinary tracts, a waning of function, and a progressive dilatation of collecting components. In the face of the seeming hopelessness of the urological situation in these patients, reevaluation of the occasional startling success attending sacral exploration of meningomyeloceles repaired at birth (wherein denudation of the scar and adhesion attendant upon the previous operation has been followed by an ameliorative change in the vesical functional state) stimulated a reassessment of certain of our cases of meningomyeloceles, operated on at birth and subsequently incontinent, with a view toward sacral exploration and lysis of adhesions, in the hope that improvement in vesical function might result.

Within the past 2 years, five patients with meningomyeloceles from 6 to 26 years subsequent to early operation, and still suffering varying degrees of urinary and fecal incontinence, have been afforded sacral exploration with the purpose of resection of such scar or adhesion as might be attendant upon the previous operation.

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CASE 1.—A 19-year-old white youth had been born with a meningomyelocele, which was repaired shortly after birth. The urinary history was that of constant leakage during the day, with involuntary voiding of large amounts at fairly regular intervals at night. When the patient was asked to urinate, with straining he could void a small amount of urine, but customarily he would dribble urine almost continually, especially with any increase in intra-abdominal pressure. The bladder capacity varied between 300 and 500 cc. No urinary residuum was noted. Cystography demonstrated a Christmas-tree type of bladder, studded with small cellules. Urography revealed relatively normal upper tracts. At cystoscopy there was noted moderate to marked trabeculation, detrusor hypertrophy, and mild elevation of the bladder neck. Abdominal straining was accompanied by contraction of the trigone and depression of the vesical neck. Cystometrograms delineated contractions of varying vigor with the typical resistance of the autonomous bladder to increasing increments of fluid. Sensation relative to vesical distension began at 200 cc. and continued to the point of abdominal straining at 450 cc. Blood chemistry studies were within normal limits; a Proteus urinary infection was present. The functional impression was that the patient had a bladder with good capacity, that moderately effective and sustained detrusor contractions were present, and that there seemed to be a relative flaccidity of the urinary outlet, coupled with the picture of a poor reciprocal action between the detrusor and the remainder of the bladder. In September, 1954, sacral exploration was carried out. At the site of the previous operation extensive adhesion and scarring were discovered. Two findings appeared noteworthy: First, there was no cystometric reaction to electric stimulation of any of the remaining nerve fibers amid the mass of scar. Stimulation of intact nerve

roots in the area afforded no demonstrable change in vesical muscular tonus. Second, upon relief of adhesions and scar, and with freeing of the cord, it was seen to be released from marked tension and to migrate cephalad, thus diminishing traction on the nerve roots intact above this point. In the immediate postoperative period, the patient noted a gradual diminution of incontinence, and, as of March, 1956, he remains completely continent if he maintains a one-and-one-half- to two-hour voiding schedule. There has been no demonstrable urinary residuum; the urine is not infected, and excretory urograms depict normal upper tracts. The bladder capacity is 550 cc. The cystometrogram depicts less detrusor resistance to incremental filling. The voiding pressure is noted to be strong and well maintained. The patient's urinary stream is of good caliber and force and is easily initiated. He maintains a voiding schedule of one to two hours and utilizes abdominal straining, but not Credé's method. The patient remains dry all night every night. From a psychologic, sociologic, and functional point of view the patient is much improved.

Case 2.—A 5-year-old white girl who had been noted to have a myelomingocele at birth, and who was operated upon shortly thereafter, was seen during the ensuing years, despite attempts at toilet training, to remain completely incontinent of urine. Fecal continence had been attained by strict adherence to dietary management. During the first three years of the baby's life, repeated urinary tract infections were experienced. When the child was first seen, in 1953, she was noted to have a bladder capacity of 250 cc. and a dribbling type of incontinence, associated with a urinary residuum of amounts varying from 2 to 8 oz. (60 to 240 cc.). The urine contained Aerobacter aerogenes. Urograms delineated marked ureteral and pelvic dilatation. Cystograms revealed a Christmas-tree type of bladder with many small cellules. At cystoscopy, trabeculation and some diminution in the caliber of the vesical neck were noted. In view of the urinary residuum and the purported vesical neck contracture, transurethral resection was carried out in March, 1954. Subsequent to this procedure, there was no variation in the urinary pattern, but there was significantly less urinary residuum. During this period, attempts to toilet train the child continued unsuccessfully, and she remained completely incontinent. Sacral exploration was done in October, 1954, and a tethering of the cord was noted. The lower end of the spinal cord, at the site of the previous repair, was encased in adhesions and scar and under marked tension. Electric stimulation of the scar tissue and of the nerve roots above it failed to reveal any cystometric reaction. With lysis of adhesions and denudation of scar, the cord was seen to move cephalad and to relieve the traction-tension on the more superior nerve roots. Subsequent to surgery, a gradual improvement was noted in urinary control, inciting the child's mother to even more persistent efforts to toilet train the child. Within a few months the patient was completely continent, and she has remained so. Variable, but small, amounts of urinary residuum have been seen to exist, and infection has persisted. Excretory urograms, however, show no change from those in 1953, and recent cystograms delineate no appreciable difference in contour or any ureteral reflux. In the two years since surgery, one bout of clinical urinary infection has occurred. We find that the child now has a fair amount of bladder sensation and that, by maintaining a voiding schedule of approximately two hours, she can remain completely continent. There has been, occasionally and very sporadically, nocturnal enuresis. The most recent cystometrogram demonstrates what is ostensibly an autonomous bladder, but one of good capacity, with a powerful voiding pressure. Despite the persistance of urinary residuum, it has been with trepidation that we have contemplated further vesical neck revision, in view of the fact that the child is now continent and that no change in the upper urinary tract has been seen to occur. Transurethral resection will in all probability be carried out in the future and perhaps will be coupled with ureteroplasty.

Case 3.—A 14-year-old white boy was first seen at the age of 7 years, for what was described as frequency of urination, nocturia, and bed wetting. He had undergone repair of a meningomyelocele shortly after birth and had been noted to have experienced urinary difficulties continually since then. Prominent in the history were, first, the perpetual odor of urine about the patient and, secondly, the necessity for him to strain to urinate. When the child was first seen, in 1947, the clinical finding was that of constant dribbling of urine. It was determined that the patient's bladder capacity was small, that there was some sense of bladder distention, and that with abdominal wall contractions there would be urinary leakage. Variable amounts of urinary residuum were found. Since a relatively small urethral meatus was present, a meatotomy was done, subsequent to which the average urinary residuum diminished. At cystoscopy a moderate amount of bladder trabeculation and gaping ureteral orifices were noted. Excretory urograms, which were normal initially, began in 1951 to show gradual dilatation of the upper tracts, and cystograms delineated ureteral reflux on the left. Many clinical attacks of urinary infection were experienced, and the infection was mixed. Cystometrograms demonstrated a spastic type of bladder of variable capacity, with poor accommodation to in-

creasing increments of fluid. Sacral exploration was done in October, 1954. Again a tethered cord was found. Marked tension on the more cephalad nerve roots was evident, owing to the presence of scar and adhesion at the site of the previous repair. Electric stimulation of the scar tissue and intact nerve roots above gave no cystometric response. With lysis of the adhesions and release of the cord it was seen to move cephalad and to reduce the tension on the more superior nerve roots. The most noteworthy finding subsequent to operation was that the family noted a definite, marked, diminution in the odor of urine about the boy. There has been progressive improvement in continence during the daytime, but the patient persists in wearing a urinal when he leaves home. There has been some question as to the mental level of the patient and what bearing this factor may have on the progression toward continence. The boy continues to wet the bed one time at night, but in general he is markedly improved in respect to continence alone. Urograms show no change in the period since sacral exploration. Cystograms remain the same, but cystometrograms show a definite improvement in detrusor capabilities. The reaction of the bladder to filling is more quiescent, and the voiding pressure is good. The boy has been instructed in the use of abdominal pressure and the Credé maneuver and seems to pass a better stream. With persistent instruction and encouragement further improvement in continence may be achieved.

Case 4.—A 26-year-old white man had been born with a meningomyelocele, which was repaired at the age of 18 months. There had been incontinence of urine and feces since birth. At the age of 15 years a gracilis muscle transplant to reinforce the urethral sphincter had been attempted, apparently without any benefit. A urinal was worn during the daytime and diapers at night. When the patient was first seen the bladder capacity was noted to be adequate and a certain amount of sensation in respect to filling was noted. There was, however, poor detrusor expulsive tone and an apparent flaccidity of the sphincter mechanism, with a resultant constant dribbling. The bladder capacity ranged between 400 and 500 cc. No urinary residuum was apparent, but a Proteus infection was present. The upper urinary tracts were normal by urography. Cystometrograms revealed a moderate resistance to increasing increments of fluid. Fair expulsive force was noted at the upper limits of bladder capacity. Sensation of vesical fullness was experienced between 6 and 8 oz. (180 and 240 cc.) and definite discomfort upon instillation of 10 oz. (300 cc.). The blood chemistry studies were within normal limits. There had been no clinical signs of upper urinary tract infection. As in all of these cases, there was saddle anesthesia. In January, 1955, sacral exploration was carried out. Dense scar, fibrosis, and adhesions were found at the site of the previous operation, productive of the typical picture of a tethered cord, wherein considerable tension upon superior nerve roots existed. Subsequent to the lysis of adhesions the cord moved cephalad several centimeters, revealing the extent of the tension. Electric stimulation (square wave, 6 volts) of nerve roots and the scar tissue provided no cystometric response. Almost immediately postoperatively, there was a marked change in the patient's urinary habits. He found that he could remain dry all night. Additionally, as time went on, he could void hourly and remain dry in the intervening period. Since he is a salesman, is married, and must support himself, there was a special stimulus for attempting to achieve continence. The patient has been able to remain completely continent for two or three hours at a time, and, if he adheres to a schedule of urinating every two or three hours, he can get about without a urinal or a diaper. He continues completely continent at night. The first and most noticeable mark of improvement was the disappearance of the odor of urine about him. As of June, 1956, his excretory urograms are normal, his cystogram is normal, and the cystometrogram shows a more normal reaction to increasing increments of fluid and somewhat better expulsive tone. There is no urinary residuum, and the urine is uninfected. The blood chemistry studies are within normal limits. The patient's only lapse from almost complete continence has been in the recent past, during a period of economic crisis; he apparently failed to adhere to any schedule of urination and overstretched the limits of his improved bladder function. He has in general done exceptionally well from a continence point of view.

Case 5.—A 13-year-old white boy had been born with a meningocele, which was operated upon two to three months after birth. The patient was incontinent of urine and feces with additional defects of an arrested hydrocephalus and bilateral talipes equinovarus. When the boy was first seen, in 1952, a gracilis muscle transplant to the anal canal was carried out, which has since seemed to be partially successful. The picture of vesical function was that of continued dribbling, accentuated by movement. If the boy would remain supine, there was apparent continence for perhaps as much as an hour, with a subsequent autonomous emptying of the bladder. There was no sensation of bladder fullness and no awareness of urine loss. The boy was kept in diapers. The bladder capacity was noted to be very small, approximately 3 to 4 oz. (90 to 120 cc.). The detrusor was spastic

and incompetent in respect to cohesion of expulsive force. Urinary residuum averaged approximately 1 to 2 oz. (30 to 60 cc.). At cystoscopy a urethral meatal stenosis was noted; there was extensive trabeculation, cellule formation, and a contracture of the vesical neck. Cystograms depicted a Christmas-tree type of bladder, with cellulation and trabeculation, and left ureteral reflux. Excretory urograms demonstrated normal upper urinary tracts with the exception of a very mild dilatation of the juxtavesical ureters. A mixed type of urinary infection was present. Blood chemistry studies were within normal limits. Sacral exploration was done in October, 1955. Extensive adhesions and scarring were found at the site of the previous operation, and the cord was seen to be under marked tension, typical of the tethered cord. With release of the adhesions, the cord moved cephalad 1.5 to 2 cm. During the dissection there was no cystometric response to nerve stimulation. In the immediate postoperative period it was noted that there was a marked increase in bladder capacity, at an average of 10 to 12 oz. (300 to 360 cc.). There was however, persistence of urinary residuum, and therefore transurethral resection was carried out in October, 1955. After removal of the catheter, there was a short period in which diminution in bladder capacity and constant dribbling reappeared. Shortly thereafter a marked increase in bladder capacity occurred as well as the achievement of continence, even in the face of abdominal contraction, for periods of an hour to an hour and a half. Perhaps the most marked immediate change was the appearance of complete continence at night. Postoperative cystometrograms revealed an increased capacity, a more quiescent attitude toward incremental filling, and a more cohesive expulsive tone. The parents are overjoyed at the fact that the patient can stay dry all night and that the odor of urine around the house has diminished so perceptibly. The boy has been kept on a voiding schedule of one and one-half to two hours and, with the exception of occasional accidents, seems to be progressing well.

Comment

In assessing what has been achieved in these five patients, most startling is the appearance of partial or complete continence postoperatively. It would seem tenable, in view of the complete saddle anesthesia exhibited in each of these cases, that a total disruption of sacral reflex arcs must pertain and that there could be no parasympathetic or somatic nerve connections between the spinal cord and the bladder. Residuary cord innervation would then stem from the sympathetic outflow of T-12 and L-1. Could there be any affect relative to vesical innervation from resection of scar in an area not only visibly devoid of functioning nerves but obviously dissociated from vesical connection since the neonatal repair of the congenital neurovertebral defect? Resection of scar should neither add nor detract functionally, in relation to sacral nerve innervation, in view of the absence of sacral nerve roots. The lack of cystometric response, in every case, to maximal electric stimulation would seemingly verify the grossly evident deficiency of sacral nerve root vesical connections.

Emmett [1] has contended that, in most instances of this nature, vesical functional changes (as were seen in Alexander's [2] case) following sacral exploration and resection of normal or abnormal sacral nerve connections are simply the result of a conversion of an incomplete infranuclear lesion to a complete one, with the production of a true autonomous bladder. Our functional results might have been explained on this basis were it not for the existence in each person of a complete infranuclear lesion, even prior to our exploration.

It would then seem that we must look elsewhere for an explanation of the results of the operative procedure. In each of these cases, the spinal cord was tethered by the scar tissue of the previous operation, and under marked tension. That this tension had increased as the skeletal framework grew, and had produced traction on the nerve roots as they entered and left the spinal cord was revealed by findings of progressive neurological deficits other than vesical and rectal. With surgical relief of this tension, it would seem reasonable to expect a general improvement in nerve conduction. In respect to vesical function, since sacral roots could not be implicated, in what manner could such improvement be mediated? Apparently only via sympathetic innervation. It could then be postulated

that relief of traction on the spinal nerve roots might be permissive of a more normal sympathetic outflow with, theoretically, the possible subtended establishment of a reflex arc for the bladder via the T-12 L-1 outflow and fasciculi proprii segmentally in the cord.

The mechanism for the production of continence in Alexander's case (subsequent to sectioning of S-3 nerve roots) must be at variance with that in our cases. Alexander postulated that sectioning of S-3 had blocked abnormal parasympathetic outflow, permitting a more effective coordination and mass contraction of the detrusor in response to physiologic filling of the viscus. To transpose this theory as an explanation for the results achieved in our cases seems unreasonable in view of the absence in Alexander's case of any signs of tension or traction at the site of the previous meningomyelocele repair. Additionally, Alexander noted that, despite a certain amount of saddle anesthesia in his case, there was cystometric response to electric stimulation of the nerve roots, indicative of an intact sacral arc. In our patients, no such nerve supply could be demonstrated grossly, microscopically, or by stimulation. It would thus be difficult to contend that our results were obtained by a blockage of abnormal parasympathetic outflow.

If our theorization is in any sense correct, the classic views regarding sympathetic innervation, particularly as studied by Learmonth,[3] may be adduced in its support. If in reality the sympathetic influence on vesical function is inhibitory to the detrusor, and motor to the trigone and internal sphincter, the findings in these patients can be more readily explained on the basis of a return to a more normal sympathetic activity subsequent to release of traction-tension and the obviation of any attendant ischemia.

Our findings are in concurrence with those of Morales[4] in that neither before nor after surgery is the powerful sustained contraction of the normal detrusor achieved. These are not normal bladders postoperatively; yet apparently a more competent relationship has been established between the vesical neck and the more quiescent and cohesive detrusor. Postoperatively, it would appear, as reflected by cystometric and other functional studies, that these are more competent bladders; less susceptible to external stimuli (intra-abdominal pressure and movement) and markedly less resistant to stretch (incremental filling).

Is there actually any increased peripheral resistance, in the form of increased vesical neck tone? In view of the fact that transurethral resections were carried out in two patients (theoretically compromising the efficiency of an increased tonus) it would appear that an increased peripheral resistance could not be promulgated as the basic etiology for the achievement of continence. In essence then, what seemingly has occurred is a return to a more competent reciprocal relationship between the detrusor and the peripheral resistance, which, as Watkins[5] has stated, is partially a mechnical resistance from the pressure and elasticity of the tissues surrounding the urethra in the region of the triangular ligament.

That a cord connection with the bladder permissive of a positive innervative effect may have been reestablished may be further postulated from the fact that when these persons are subjected to nervous tension they frequently will again temporarily lose control of urine. Could this be suggestive of a sympathetically mediated stress dysrhythmia between detrusor and outlet, indicative that sympathetic control of detrusor activity is now a prominent one, and further evidencing that by release of traction a spinal cord connection with the bladder has been reestablished? Such explanatory summarization is of course suppositious.

One point seems unquestioned, that regardless of the interpretation, these patients have achieved continence. A most beguiling hypothesis as to the reason for the production of this continence would seem implicit in the release of spinal cord traction.

Despite the fact that socially and psychologically these patients have been much improved, from a urologic point of view many serious problems continue to present themselves. Although the neurologic lesions were all rather similar, urologically each person showed definite variations. Functional and radiographic evaluations of the urinary bladder in neurovesical dyskinetic cases cannot be taken as valid portrayals of the status of the upper urinary tract. As was seen here, trabeculation, cellulation, and marked bladder deformity can be associated with a relatively normal upper urinary tract, whereas the reverse may easily obtain.

Although the existence of hydronephrosis and ureteral dilatation is of great concern, of perhaps greater import is ureteral reflux. As Graves and Davidoff have mentioned, where bladder deformity and a resistance to stretch occur, as is customarily observed in patients of this sort, ureteral reflux will more commonly occur as a result of this resistance to bladder filling. We had hoped that in the cases where reflux was noted preoperatively there might be an amelioration or cessation of this postoperatively. This has, however, not happened.

That these persons are in a precarious condition is reflected by the rapidity with which upper urinary tract deterioration can supervene. In one of these patients, although complete continence has been achieved, it would appear that there has been functional and architectural worsening in the postoperative period. Thus we cannot say that we have achieved in any of these patients more satisfactory vesical function in respect to an assurance of optimum urinary drainage. These factors bear out the necessity for continued observation of these patients. We cannot allow success in the production of a dry patient to obscure architectural and functional deterioration necessitative of further therapeutic endeavor. In one of these patients ureteroplasty with possible prolonged cystostomy drainage is contemplated. In another further transurethral resection of the vesical neck may be necessary in an attempt to do away with urinary residuum and concomitant infection. In respect to the various sphincter operations which have been done in the past, it would seem reasonable, in view of the success of preliminary operative measures in this specifically tethered cord problem, that, with the release of tension and with the institution of a greater measure of continence, a subsequent sphincter operation to further increase peripheral resistance might afford better results than have been previously obtained.

In respect to the comment of Morales regarding the futility of bladder training in these persons, it has seemed to us, despite the fact the patients have never been cognizant of any ability to open or close urinary or rectal sphincters, that by approaching the problem obliquely—beginning merely with a voiding schedule, a regulation of fluid intake, and then the utilization of various methods of initiating and perpetuation of urination, such as abdominal straining and the Credé maneuver—these methods have been very successful in fortifying such muscular control as exists. Further, these patients have been afforded a certain amount of courage in respect to an increasingly continent status in society. It is apparent that the fewer mistakes they make the more convinced they are that they can remain continent and the greater is their desire to do so. Whether there is any suprasegmental assistance, mediated via the remnants of cord innervation to the bladder, is doubtful; the greater likelihood is that the muscles themselves are trained much in the way the lower bowel evacuates itself at a certain time each day in normal persons.

It is our intention to follow these patients closely and to report upon them at intervals not only in respect to their status regarding continence but in reference to such urologic complications as may have beset them.

Although the restitution of continence in so small and specific a group offers no panacea for the amelioration of incontinence in general, it would appear that a more vigorous approach to the spina bifida problem would result in the unearthing of

more of such tethered cord cases, with, presumably, surgical results as encouraging as those presented here.

Summary

In certain of the severer types of spina bifida requiring neonatal reparative surgery a condition may later develop which can be called the tethered cord syndrome.

Relief of the traction found in the tethered spinal cord, by sacral exploration and lysis of scar, not only has ameliorated peripheral neurologic defects but has resulted in the restitution of continence in five patients. The postulation of a sympathetic nervous system assumption of vesical control as the etiologic mechanism in the production of continence is discussed. Deleterious urologic residua of the neurovesical dysfunction in the five patients presented are outlined. Advocation of operative investigation in spina bifida patients who have undergone previous surgery is proposed, with the hope that the tethered cord syndrome outlined here may represent a curable neurovesical lesion.

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Severe Hemorrhage Following Gastrectomy

A Survey of the Literature Relating to Its Frequency, Mortality, Prevention, and Treatment

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Serious upper gastrointestinal hemorrhage has occurred as a postoperative complication in 2 of the last 100 consecutive subtotal gastrectomies performed at the Syracuse Veterans Administration Hospital. These cases, which are reported at the close of this article, aroused our interest in this complication. A survey of the literature revealed that there is little information about bleeding as a postgastrectomy hazard in the American surgical literature. This study is designed to determine the actual incidence of this complication and the mortality associated with it and to discuss its etiology, prevention, and treatment.

Incidence

In 1946, Bruusgaard[1] discussed gastrointestinal hemorrhage and reported 11 postoperative hemorrhages in 578 gastric resections, an incidence of 2%. By utilizing all available series which report operative complications following gastric resection,[1-38] we have obtained the occurrence rate of serious postoperative hemorrhage. Of 10,919 gastrectomies, 111 involved serious postoperative hemorrhage—an incidence of 1%. Serious hemorrhage occurring more than 21 days after gastrectomy was arbitrarily discarded since marginal ulceration seemed a likely cause, and this study does not propose to include late complications

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The deaths due to hemorrhage reported in the 10,919 gastrectomies, when combined with such deaths in 3405 gastrectomies collected from other series reporting mortality but not morbidity,[39-49] number 14. The mortality calculated from the total collected series of gastrectomies (14,324) is 0.1%.

It is thus seen that the incidence of serious postoperative hemorrhage following subtotal gastrectomy is about 1% and that 1 patient in 10 having such a complication may be expected to die from it.

The incidence of severe postoperative gastrointestinal hemorrhage in the series we have reviewed varies from 0% to 7.8%. However, in the studies reporting on at least 300 cases, the incidence ranges from 0.8%, reported by Christmann,[34] to 2%, reported by Bruusgaard.[1] By way of comparison, the National Survey by the American Gastroenterological Association[50] reports six postoperative hemorrhages within 30 days following 468 gastric resections, an incidence of 1.3%.

Etiology

The sources of postgastrectomy hemorrhage most frequently reported are (1) The anastomotic suture line, (2) a remaining or overlooked ulcer, (3) postgastrectomy gastritis, (4) the duodenal stump suture line, (5) new gastrojejunal ulcer, (6) hemorrhagic diseases, and (7) jejunogastric intussusception.

The number of cases in which the findings at reoperation or autopsy have been reported is very small (Table), and no

*Sources of Hemorrhage in Sixteen Reexplored Cases and Three Autopsies**

	Cases, No.
Anastomotic suture line	8
(3 from Hofmeister suture line[20,51])	
Duodenal stump or retained ulcer	5
Gastritis	3
Not found	1
Not reported	2
Total	19

* References 1, 17, 19, 21, 31-33, 35, 36, 38, 53, 54 and Case 2.

definite conclusions can be drawn regarding the relative frequency of the sources of bleeding. It is our feeling, however, that improperly ligated vessels on the gastric side of the anastomosis or a duodenal ulcer left in situ is the most common cause of bleeding in the early postoperative period. By contrast, acute gastritis or slough of the tissue incorporated in a hemostatic suture at the anastomotic line is more apt to cause bleeding during the second and third postoperative week.

The anastomotic line is believed by European authors to be the most common source of bleeding.[1,17,51,52] Many techniques have been proposed to obtain hemostasis, including cautery, utilization of various special clamps, omission of all clamps, exposure of cut edges to air, and the use of three rows of sutures. Many German surgeons stress the importance of careful ligation of the gastric vessels by the von Haberer technique,[57-59] but they disagree as to whether or not postoperative hemorrhage is always from gastric vessels or may also occur from jejunal vessels at the anastomotic line.[58,59] Our review of the various series shows no definite relationship of postgastrectomy hemorrhage to the type of gastrectomy, the use or omission of clamps, the number of rows of sutures in the closure, or the presence of benign or malignant disease.

Most of the hemorrhages occurred within a few days of the operation, but there were a few which appeared around the 10th day.[2,3,20,38] The latter probably were due to gastritis or to necrosis and sloughing of the inner layer of the anastomosis.

Prevention and Treatment

Prevention of this complication demands that accepted standard surgical principles be applied to the gastrojejunal anastomosis: (1) individual ligation of bleeding points; (2) placement of the stoma in the antimesenteric line of the jejunum; (3) avoidance of folds in the closure, especially at the angles, and (4) a two-layer closure with use of a continuous hemostatic inner suture. Also, the duodenal stump closure must be exacting to obtain hemostasis there. Finally, when possible without endangering the patient's welfare by too energetic dissection, a duodenal ulcer should be removed with the resected duodenum to prevent postoperative hemorrhage from the ulcer bed, although it is well known that ordinarily the retained ulcer will heal without complication when it is left in situ and the acid stomach contents are diverted.

The treatment of postgastrectomy hemorrhage can be approached conservatively at first. Maintenance of blood volume by adequate transfusions and continuous gentle lavage and suction usually suffice to control the situation. Since bleeding from vessels in the suture line and from gastritis are common causes, complete decompression of the stomach pouch to allow collapse of the vessels, as in the treatment of the bleeding distended bladder, is of primary importance. Also since, according to the theory of Reymond,[56] pancreaticobiliary secretions prevent clotting when in prolonged contact with open vessels, efficient suction on the gastric pouch may contribute by preventing this additional adverse factor.

Deficiencies in the patient's clotting mechanism should be considered and corrected if present. These include lack of vitamin K, calcium, and fibrinogen.

The absorbable gelatin sponge powder (Gelfoam) thrombin treatment of Cantor[55] occasionally seems to control the bleeding. One case is reported here in which a hemorrhage of 18 hours' duration having required 7000 cc. of blood for replacement ceased

within 1 hour after the Cantor treatment was instituted (Case 1).

In the rare case, massive bleeding continues despite the above treatment and reoperation becomes imperative. If the duodenum is not suspiciously distended and discolored, an immediate gastrotomy is indicated, either through the stomach remnant or at the anastomotic line. Since visualization of the internal anastomotic line, especially in a posterior anastomosis, is rather difficult, stay sutures may be placed through opposite sides of the stomal rim and used to pull the anastomosis into view. If a bleeding vessel or vessels are found and individual ligation is not satisfactory, the bleeding area can be oversewn with a continuous interlocking absorbable surgical (gut) suture of chromic type.

When the duodenum is distended and discolored with blood, or when the bleeding is seen to be coming from the afferent loop at gastrotomy, the bleeding source is most likely a retained ulcer or the duodenal suture line. In either case, it is necessary to open the duodenal closure to determine the source of bleeding. Bleeding from the suture line can be easily controlled by suture ligature.

Hemorrhage from a retained ulcer is a more difficult problem. Further mobilization of the duodenum with resection of the ulcer is most certain to control such bleeding. When the condition of the patient or technical factors make this arduous procedure impossible, suture of the ulcer base, absorbable gelatin sponge packing, or ligation of the pancreaticoduodenal artery may control the hemorrhage.

After a duodenal stump is opened, a satisfactory secondary closure may be impossible, and establishment of a tube duodenostomy is indicated.

When massive hemorrhagic gastritis is the sole cause of hemorrhage found at operation, the only solution is a higher resection, despite the fact that these patients are often very poor risks for such a procedure.

Recurrence of hemorrhage after successful conservative therapy does not in itself indicate surgery. In one case with bleeding on the 10th postoperative day after gastrectomy, profuse bleeding recurred in 5 days and then again in 4 days; all episodes were treated with transfusions and suction, and the patient recovered.[2]

Report of Cases

CASE 1.—A grocer 63 years of age was admitted with duodenal ulcer symptoms of eight years' duration complicated by two episodes of severe hematemesis during the previous two years. Examination showed epigastric tenderness and a blood pressure of 235/130. Gastrointestinal x-rays demonstrated marked scarring of the duodenum with an active bulbar ulcer. Six weeks of hospital management resulted in healing of the ulcer crater as shown by a gastrointestinal series, but symptoms of occasional pain persisted.

A Hofmeister subtotal gastrectomy with retrocolic gastrojejunostomy was done utilizing Payr clamps. There was no active ulceration present. The duodenal stump was closed with an inner continuous absorbable surgical (gut) suture of chromic type and an outer row of interrupted nonabsorbable surgical (silk) Lembert sutures. Bleeding points at the anastomotic line were individually ligated. The anastomosis was performed with an inner continuous suture of chromic gut sutures and anterior and posterior rows of interrupted (silk) sutures.

Convalescence was uneventful until the ninth postoperative day, when severe hematemesis occurred. Fresh blood was aspirated continuously from the stomach by Wangensteen suction for 18 hours, and 14 units (7000 cc.) of blood were given during that period. Bleeding, clotting, and prothrombin times were normal. Instillations of absorbable gelatin sponge powder and thrombin solution were then begun, according to the method of Cantor,[8] and within one hour no further bleeding was apparent. Subsequent recovery was uncomplicated.

CASE 2.—A 62-year-old unemployed white man was admitted with a history of duodenal ulcer of two years' duration demonstrated several times by gastrointestinal x-rays. Five weeks before admission, the patient had been treated at another hospital by Wangensteen suction and antibiotics for a perforation of his duodenal ulcer. Symptoms of marked pain and low-grade partial obstruction had been un-

relieved by medical therapy since the perforation. Physical examination was unremarkable except for epigastric tenderness. Gastrointestinal series showed a bulbar ulcer, which subsequently failed to heal completely after five weeks of hospital ulcer management including hourly night feedings.

A subtotal gastrectomy was done with use of the same technique as described in Case 1. Owing to the marked inflammatory reaction and adherence of the ulcer bed to the pancreas, the duodenal stump had to be closed proximal to the ulcer, which was left in situ. Very little blood was aspirated from the stomach for the first 10 hours postoperatively, but then a continuous flow of fresh blood began through the Levin tube. Eight units (4000 cc.) of blood were required in the following six hours to maintain the vital signs and hematocrit value at normal levels. There was no decrease in the bleeding, and hence an emergency gastrotomy was done. There was very slight bleeding from a few areas of the gastric mucosa, which gave the appearance of hemorrhagic gastritis, but there was no bleeding from the anastomotic suture line. The duodenal stump closure was intact. Fresh blood in large amounts and clots were seen coming from the afferent loop. It was felt that the bleeding was from the duodenal ulcer left in situ. The very poor condition of the patient precluded duodenal mobilization and further resection; hence a double jejunostomy was done in the efferent loop about 4 in. (10 cm.) distal to the anastomosis. The proximal tube was placed through the stoma into the afferent loop, and a feeding tube was placed distally. Postoperatively, frequent irrigations and continuous suction of the proximal jejunostomy tube were carried out. There was a rapid decrease in bleeding, and within a few hours only clear biliary drainage was present. Recovery was thereafter uneventful. Bleeding, clotting, and prothrombin times were normal throughout the hospital course.

Summary

The incidence of severe upper gastrointestinal hemorrhage in the early postoperative period following subtotal gastrectomy has not been determined for large numbers of cases. We review 14,324 gastrectomies from the literature and show the incidence of this complication to be 1%. There is a 10% mortality when this type of hemorrhage occurs.

The source of such bleeding is usually the anastomotic suture line or a retained duodenal ulcer. Prevention of such hemorrhage is discussed and is shown to involve standard surgical principles. A method of treatment is outlined, and nonoperative methods are shown to be successful in stopping the hemorrhage in most cases.

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Atrial Septal Defect

Experiences with One Hundred Cases Treated Surgically

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Atrial septal defects have been shown to be one of the commonest single congenital cardiac abnormalities. Many of these defects are well borne during infancy and childhood and do not manifest themselves until adult life. The pattern of symptomatology then is one of progressive reduction in myocardial reserve, followed by the gradual appearance of cyanosis and, finally, death due to a combination of right heart failure and increasing systemic anoxia.

On the other hand, as reported previously by Downing and Goldberg,[2] a very sizable number of infants suffer severely and die from this disease during the early months of life. Other children survive but exhibit marked degrees of physical underdevelopment due to an insufficient systemic circulation. A somewhat larger number experience sharp limitations in myocardial reserve, being unable to "keep up" with their fellows on maximal physical exertion, although quite comfortable at rest.

Abnormalities of development of the interatrial septum may result in one of several types of persistent transseptal communication. Excluding probe-patency of the adequately guarded (valved) foramen ovale, by far the commonest of these is the so-called "ostium secundum" defect. In this condition, one may assume either that the septum primum has undergone excessive resorption or that the development of the septum secundum has been inadequate or incomplete. In either event, the opening which remains may be considered to be a greatly enlarged foramen ovale[3] in which there is no foraminal valve capable of impeding free transseptal flow should there be a differential in the pressure levels within the respective atria.

The so-called "ostium primum" defect generally[3,4] is considered to be due to failure of the septum primum to fuse with the structures developed from the endocardial cushions (the primordia of the atrioventricular valves). Watkins and Gross[5] prefer the term "endocardial cushion defects." Thus, they group the "ostium primum" defects with other more primitive developmental abnormalities which occur in this region, such as atrioventricularis communis. In any of these conditions, the atrioventricular valves are prone to be deformed, and frequently they are found to be incompetent.

In some patients there is almost complete absence of the interatrial septum, although some residual lace-like strands of septal tis-

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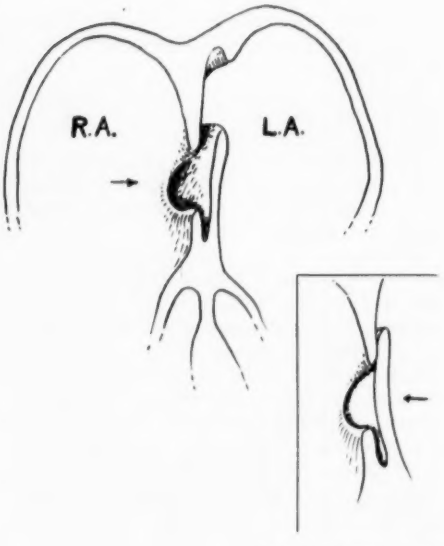

Fig. 1.—Upper left, "probe patency" of a patent but functionally competent foramen ovale (seen from the left side). Upper right, ostium secundum defect of central type which may be considered as a greatly enlarged foramen ovale. (Reproduced from Bailey, C. P.: Surgery of the Heart, Philadelphia, Lea & Febiger, 1955, p. 274.) Lower left, great interatrial defect with residual septal strands. Lower right, diagram showing effect of increased right atrial pressure which allows flow of blood through an otherwise competent foramen ovale. A higher left atrial pressure closes the valve, shutting off further flow (inset).

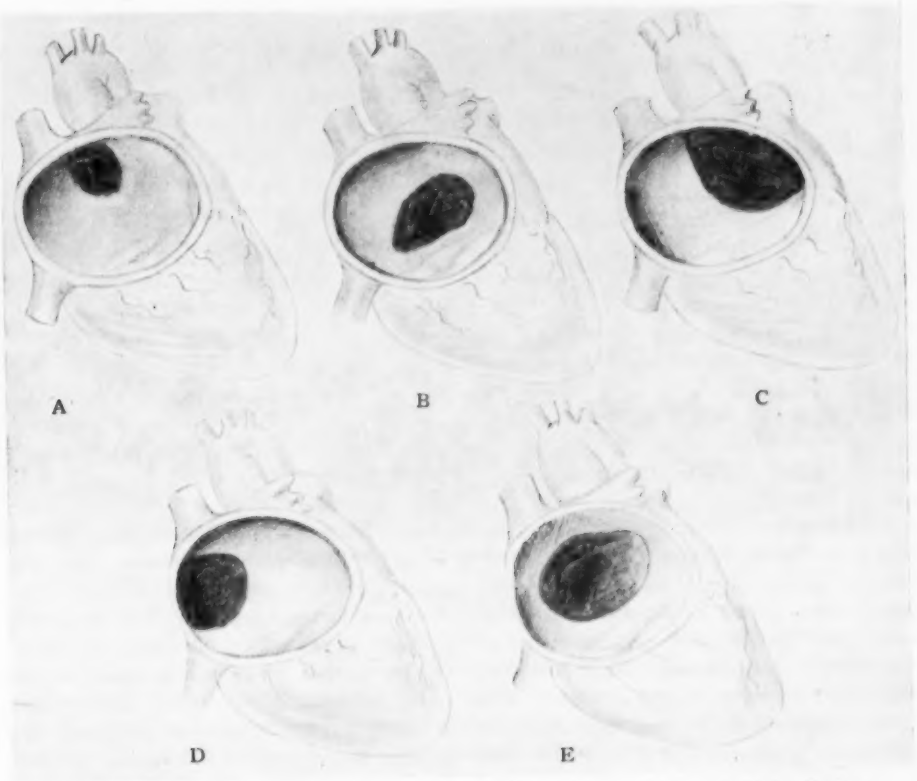

Fig. 2.—Diagrams of locations of defects of the septum secundum. *A*, high; *B*, low; *C*, anterior; *D*, posterior; *E*, central.

sue may remain. In addition to those patients who present probe-patency of the foramen ovale, there are others with a true sizable foraminal opening which, however, is guarded by a competent valve (against left-to-right shunts). These openings are not of clinical significance unless the right atrial pressure rises sufficiently to force the valve open and produce a right-to-left shunt (Fig. 1, upper left and upper right). The secundum defects may be variously located (Fig. 2). In our own series reported here, 83 of the defects encountered were of the secundum type and were classified in five groups according to location. Of these, 27 (32.5%) were located in the central portion of the septum; 12 (14.5%) were found high in the septum, practically at the mouth of the superior vena cava; 12 (14.5%) were low and seemed to encroach upon the orifice of the inferior vena cava; 16 (19.2%) were located posteriorly, there being no ridge or remnant of septal tissue between the ostia of the right pulmonary veins and the right atrium, and 9 (10.9%) made up the anterior group, in which there is little or no septal remnant anteriorly in the region of the first portion of the aorta. There were seven (8.4%) cases in which the operating note description did not accurately locate the defect. In each of the secundum types, there is at least a small but clearly definable ridge of septal tissue lying between and above (cephalad to) the two atrioventricular valves.

The posterior defects frequently were associated with anomalous drainage of the right pulmonary veins into the right atrium.

In eight patients a true stenosis of the mitral valve coexisted with an interatrial septal defect, thus completing the syndrome described by Lutembacher [6] in 1916.

Physiological and Clinical Significance

Regardless of the type of anatomical defect, a transseptal flow or shunt of blood will take place between the two atria if there is a differential between their respective pressure levels. Since the pressure within the left atrium normally is higher than that in the right, a predominant left-to-right shunt will develop in most of these persons. However, should such a defect be found in association with one of several types of congenital or acquired circulatory defect, the mean right intra-atrial pressure might be higher than the left. Then, the predominant direction of shunt must be from right-to-left, causing an admixture of venous and arterial blood within the left atrium with consequent lowering of the level of oxygen saturation of the mixed systemic arterial blood. In severe cases this produces clinical cyanosis. The classical combination of congenital lesions in which this phenomenon may be seen is congenital pulmonic stenosis (so-called "pure") in association with valvular patency of the foramen ovale. Here, the right ventricle can evacuate its blood content through the obstructed pulmonary valve only with difficulty. The end-diastolic pressure within the ventricle tends to rise, impeding and hampering filling from the right atrium. In response, this latter chamber becomes hypertrophied and capable of generating a higher internal pressure, which may exceed that of the left. This pressure forces open the foraminal valve and produces a right-to-left shunt.

Because of the excessive flow through the right atrium, right ventricle, and pulmonary arteries which a large left-to-right shunt imposes, all three vascular compartments become dilated and the muscular ones become hypertrophied. Hence, right ventricular preponderance or "strain" is common in the electrocardiograms of these patients. In contrast, the left ventricle and aorta remain small and may even appear to be atrophic. These observations have led certain authors to speculate whether the condition should not be considered as one of primary hypoplasia of the left side of the heart and aorta.

Reversal of Flow Due to Pulmonary Vascular Pathology

The excessive flow of blood through the pulmonary vascular bed which is necessitated by the existence of a large left-to-right shunt produces dilatation of the hilar blood vessels, which may be radiographically marked (Fig. 3), perhaps with fluoroscopically visible vascular pulsations, and is prone to cause pulmonary hypertension. The latter may be mild or nonexistent in early life, but it tends to become more severe with the passage of time. This finding may be construed as evidence of an increased pulmonary vascular resistance which imposes an additional burden upon the right ventricle. The increasing difficulty in evacuating the blood content of this chamber is reflected in an impedance to right ventricular filling. Hence, the pressure within the right atrium rises progressively, tending first to reduce and later to reverse the original left-to-right shunt.

While some have postulated that the first appearance of pulmonary hypertension may be due to a reversible spastic condition of the arterioles, it is evident that subsequently changes may take place within the vessel walls which are progressive and irreversible.[7-9] These changes are not dissimilar to those which are seen in the renal arterioles in systemic arterial hypertension—medial thickening, intimal hyperplasia, and progressively advancing reduction in luminal size, eventually to the point of actual obliteration. Once this end-stage condition has been reached, the septal defect, by permitting diversion of a significant portion of the systemic venous blood from the largely obstructed pulmonary vascular bed, acts in a "compensatory" capacity, relieving the right ventricle of a portion of its burden. Surgical closure of the defect at this time nearly always results in death due to right ventricular

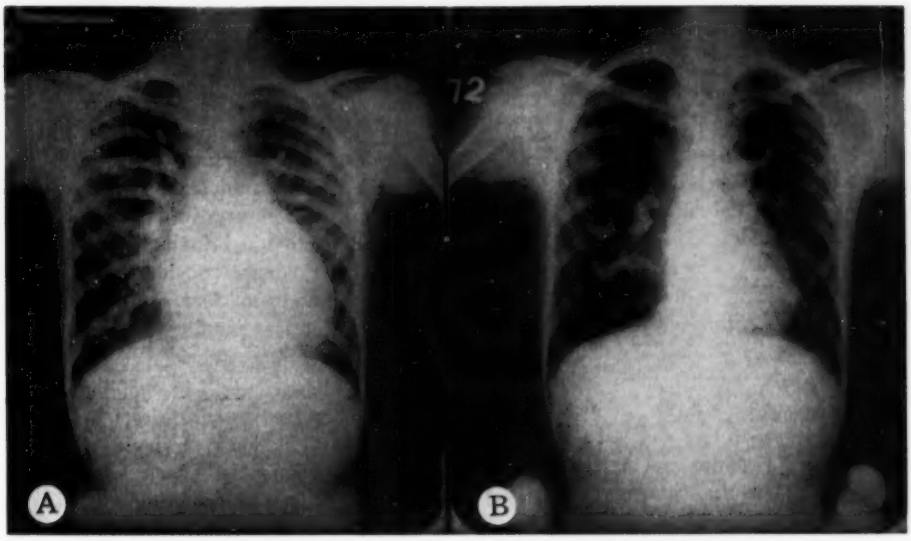

Fig. 3.—X-rays of a patient showing (*A*) increased vascular markings and cardiac enlargement prior to surgery and (*B*) marked reduction in pulmonary vascular markings and decreased heart size 10 months postoperatively.

failure. Actually, this usually is true also in cases of right-to-left shunt through an atrial septal defect which is associated with another congenital defect (such as pulmonic stenosis) unless the latter can be corrected at the same operative session.

The gradual development of pulmonary hypertension and pulmonary vascular changes in these patients is largely responsible for the clinical deterioration and eventual death, which often occurs before middle life [2] even in those who have had few or no symptoms in childhood.

Diagnosis

A history of frequently repeated pulmonary infections during early life commonly is elicited in these persons. Retarded general physical development (gracile habitus) occasionally is present. The occurrence of bouts of paroxysmal auricular tachycardia is suggestive. There may be a history of transient cyanosis during periods of physical stress. Shortness of breath upon exertion and easy fatigability are the commonest symptoms. Other evidences of lowered cardiac reserve are usual but not constantly found. Fluoroscopic or radiographic examination if the chest usually reveals dilated main pulmonary arteries and generalized congestion. The electrocardiogram often reveals a right ventricular preponderance or "strain" pattern (58% in our series). Twenty-one per cent of our patients had a right bundle branch block.[2] A cardiac murmur may or may not be present. Characteristically, it is a rather soft systolic murmur heard best in the "pulmonary valvular" area. However, it may be harsh, resembling that of pulmonic stenosis. A diastolic murmur is less common, but may be present. In the very low "endocardial cushion" defects, the harsher systolic murmur of tricuspid or mitral insufficiency not infrequently dominates the auscultatory picture. When a ventricular septal defect coexists with one of these primitive deformities, an even harsher murmur is heard, frequently associated with a systolic thrill localized over the lower sternal region.

Angiocardiography has been used to demonstrate these defects. However, a properly performed right cardiac catheterization nearly always will indicate the presence of

an atrial septal defect when a left-to-right shunt is present by revealing an increase in the oxygenation of the right atrial blood over that in the venae cavae. The only other condition in which this oxygen "step-up" is found is anomalous pulmonary venous drainage (which usually is found in association with an atrial septal defect). Cardiac catheterization provides information as to the level of the pulmonary arterial pressure and permits calculation of the pulmonary vascular resistance. In patients with coexisting or preponderant right-to-left shunts, the degree of desaturation of the peripheral arterial blood will provide a basis for measurement of the amount of this flow. In many patients, during examination the catheter may be seen under the fluoroscope to pass through the defect to enter the left atrium and perhaps even a pulmonary vein.

In our experience, it usually has not been possible to determine the location of a defect or even, in most cases, to differentiate between those of the primum or secundum type prior to operative digital examination of the septum. Occasionally, the fluoroscopic observance of the passage of a loop of the catheter through the defect has indicated that it is unusually large. In others, the direct passage of the catheter from the right atrium into a right pulmonary vein has established the presence of anomalous pulmonary venous drainage. The presence of a harsh systolic murmur near the lower portion of the sternum or catheterization evidence compatible with tricuspid or mitral insufficiency suggests that the defect may be of the "ostium primum" ("endocardial cushion") type.

Development of Surgical Methods

Cohn,[10] in 1947, was able to close artificially created interatrial septal defects in mongrel dogs by invaginating the right atrial appendage and approximating it to the margin of the defect with mattress sutures placed at each quadrant. He then detached the invaginated portion of the atrial wall by a snare technique after approximating the portion of the right atrial wall which was to be preserved above this area with mattress sutures.

Murray,[11] in 1948, proposed anteroposterior approximation of the atrial walls in the region of the septum by passing long threaded needles in the plane of the septum. Tying down the sutures in mattress fashion proved ineffective in bringing about closure because the guidance provided by external landmarks was insufficient, and direct guidance by an intracardiac finger was not practiced.

Swan and associates,[12] in 1950, attempted to close interatrial septal defects by simultaneous invagination of both auricular appendages upon plastic buttons, thus approximating them against the defect.

Dodrill,[13] Kiriluk and associates,[14] and Hufnagel and Gillespie [15] all suggested methods which were effective in the experimental animal but which proved ineffective in the human patient.

Bailey [16] performed the first repair of a human atrial septal defect which subsequently was confirmed by cardiac catheterization on January 11, 1952, by invaginating a portion of the redundant right atrial wall against the septum and approximating it with a continuous suture line to the periphery of the opening. This method of external suturing of the atrial wall to the septal tissues by the guidance of a finger inserted through the right auricular appendage is the simplest of the "closed" methods of correcting such a lesion, and today is the most widely employed procedure in clinical patients. This original technique and several subsequently described [17-19] logical modifications have been designated as "atrioseptopexy." All of the patients in the present series were operated upon in this fashion. The method has the great advantage that normal circulatory conditions are maintained during the performance of the operation, hypothermia or an extracorporeal circulatory system, therefore, being unnecessary.

Gross,[20] in 1953, proposed operating upon atrial septal defects with guidance by dig-

ital palpation through an open "well" of latex sutured to an opening made in the wall of the right atrium. Local heparinization of the blood in the "well" prevented coagulation during the course of the procedure. In a recent publication, however, Watkins and Gross [5] have recommended adoption of the closed external suture technique of Bailey for the majority of cases. Kirklin [21] still employs the original "well method" for most of his patients.

Sondergaard,[22] in 1953, proposed circumferential construction of the interatrial tissues with a heavy nonabsorbable suture. This was passed in accordance with certain externally evident landmarks. Björk and Crafoord [23] subsequently modified this technique by the addition of guidance by a finger inserted into the right atrial chamber by way of the auricular appendage. This method has considerable support, especially in the European countries.

Gibbon,[24] on May 6, 1953, successfully closed an interatrial septal defect under direct vision while maintaining the bodily circulation with his heart-lung apparatus.

Lewis and Taufic [25] successfully repaired an atrial septal defect under hypothermia on Sept. 2, 1952. Since then, Swan [26] has adopted the hypothermic technique.

It has been our opinion that the very considerable inherent risks associated with these "open" techniques as yet do not justify their acceptance in patients with atrial defects of the "septum secundum" type. Practically all of these lesions may be corrected safely and simply by the method of atrioseptopexy. To illustrate the intensity of our conviction: Heparinized blood had been obtained for two of the patients included within this series, and the necessary arterial and venous cannulations for a heart-lung bypass had been completed in one of them, before the diagnosis of a secundum type atrial defect was established definitely. The elaborate preparations were discarded immediately in each case, and the defects were closed by a simple atrioseptopexy procedure.

Atrioseptopexy—Principle and Technique

The basic anatomical problem in atrial septal defects is a lack or dearth of cardiac septal tissue. Unless an open method is chosen and it is found that the edges of the defect can be sutured together directly and usually under some tension, the problem resolves itself to replacing the lacking tissue by a prosthetic or by some available excess living tissue. By the digitally guided closed external suture method, a portion of dilated right atrial wall simply may be invaginated against the septal defect and then sutured accurately to its margin, thus providing the necessary substance to overcome the tissue deficit (Fig. 4). However, in some types of defect the atrial wall is sutured to only one margin of the septal tissue in such a way as to direct the flow of returning venous blood to the appropriate sides of the septum by a "baffle" effect (Fig. 5, lower left).

The placement of approximating sutures during the performance of atrioseptopexy is rendered accurate by the guidance of the left index finger inserted into the heart by way of the right auricular appendage. At the same time, the mitral valve can be explored and any coexisting stenosis relieved. A modification of the technique of atrioseptopexy of coexisting anomalous drainage of the which permits the simultaneous correction right pulmonary veins (Fig. 5). In two was devised in 1953 by Neptune et al.[17] patients (not included in this series) with isolated anomalous drainage of the right pulmonary veins, an appropriately placed septal defect was created surgically. Then, the resultant combined condition was treated as described above. When mitral stenosis coexists,[18,19] it readily may be corrected by passing a finger and/or instrument into the left atrium by way of the defect (Fig. 5, lower center and lower right).

Indications for Surgery

Originally, it was felt that patients with interatrial septal defects should not be operated upon unless they presented severe

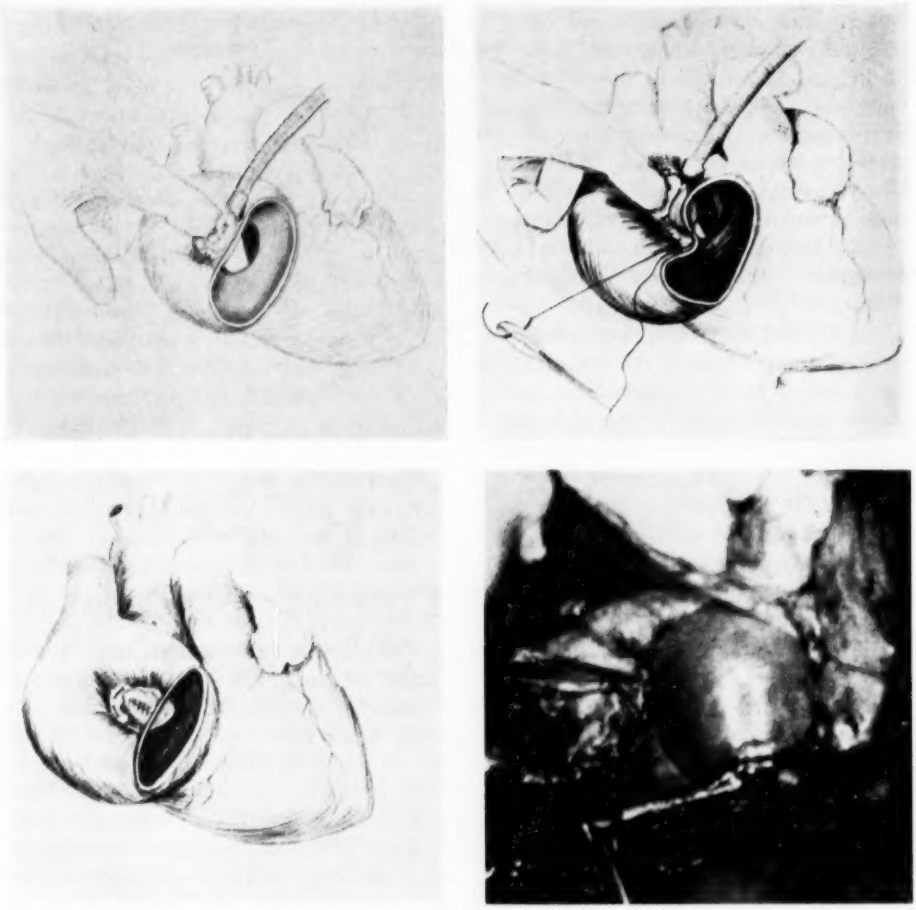

Fig. 4.—Illustration of the technique of atrioseptopexy. Upper left, digital exploration of defect via right auricular appendage and placement of initial suture, bringing right atrial wall into apposition with the inferior margin of the defect. Upper right, progressive circumferential suturing. Lower left, defect closed and site of entrance of finger closed. (Upper right and lower left reproduced from Bailey,[18] *The Journal of Thoracic Surgery*, The C. V. Mosby Company, St. Louis.) Lower right, photograph taken at completion of first closure of an atrial septal defect by the external suture method. (Reproduced from Bailey,[16] *Annals of Internal Medicine*, American College of Physicians, Lancaster, Pa.)

clinical symptomatology such as congestive heart failure. Later, this view was modified and patients were included who had relatively milder symptoms, provided the pulmonary blood flow was estimated (by catheterization) to be double that of the systemic. Significant pulmonary hypertension was considered to be a relative indication. Today, we are coming to the opinion that the mere anatomical existence of a sizable atrial septal defect of the ostium secundum type justifies the submission of a patient to atrioseptopexy, provided that a sizable and preponderant left-to-right shunt exists. Because of the inaccuracies inherent in the calculation of transseptal flow by catheterization techniques, it is felt that the left-to-right shunt must exceed any right-to-left shunt which may be present by more than 1.5 liters per minute (in an adult) before it can be considered significant. When the preponderance of left-to-right flow is less than this

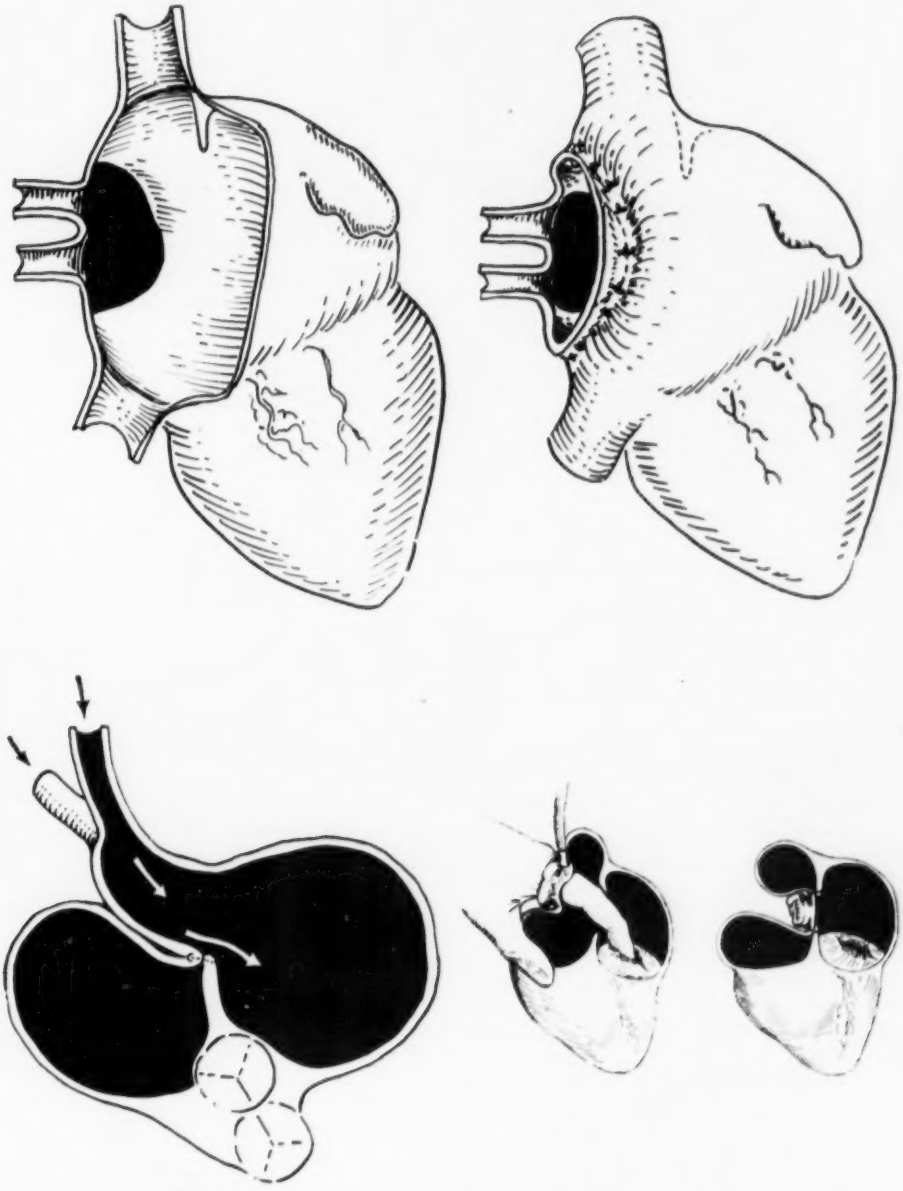

Fig. 5.—Upper left, logical extensions of the technique of atrioseptopexy. Anomalous pulmonary venous drainage into the left atrium in association with a posteriorly located septal defect. Upper right, atrioseptopexy procedure for auricular septal defect plus anomalous right pulmonary venous drainage. Lower left, sectional view (from the top) showing that the above procedure really doesn't close the defect, but merely diverts the pulmonary venous flow into the left atrium by a "baffle effect." Lower center, correction of coexisting mitral stenosis by approaching the mitral valve via the right atrial appendage and the septal defect. Lower right, subsequent closure of an atrial septal defect by external suturing.

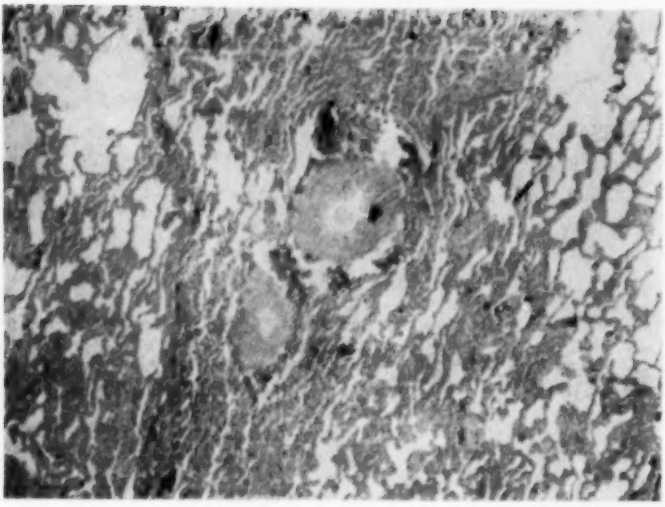

Fig. 6.—Photomicrograph showing extensive obliterative pulmonary vascular changes which may develop as a result of long-continued excessive pulmonary blood flow. Reduced about 1/3 from mag. × 26.

amount, the patient is considered to have a "balanced shunt." Pulmonary vascular hypertension now is considered somewhat as a deterrent, especially when higher than 70 mm. Hg (systolic). Nevertheless, surgery is offered to most of these patients in the hope that the vascular changes within the lung will not have progressed to the stage of irreversibility (Fig. 6).

We now believe that a patient with a preponderant right-to-left shunt or a "balanced" (equalized) shunt usually will have progressed beyond the limits of operability unless some other pertinent abnormality exists which can be relieved simultaneously. Otherwise, we must assume that the pulmonary vascular changes have progressed to the point where, even if they are not absolutely irreversible, the defect has assumed, in part, a compensatory role. Operative closure of the transseptal communication in such persons appears to carry a prohibitively high mortality.

Originally, it was felt that defects of the "ostium primum" type also might be treated by the technique of "atrioseptopexy." However, the discouraging results obtained among the 17 patients operated upon for this type of lesion (here reported) have caused us to conclude that they should be treated preferably by one of the open methods (using either hypothermia or the heart-lung bypass). One of the major causes of death among this group has been the inadvertent interruption of the common atrioventricular conduction bundle (of His) by the placement of a suture into the lower margin of the defect. It is felt that avoidance of this bundle by palpatory recognition of certain internal cardiac landmarks, such as the ostium of the coronary sinus and the central fibrous body of the tricuspid annulus fibrosus, as recommended, respectively, by Bailey [27] and by Watkins and Gross,[5] is not feasible in patients with ostium primum defects. Continuous electrocardiographic monitoring during the operative procedure may indicate the proximity of a suturing needle to the bundle, but should the latter actually be interrupted by tying down the suture, immediate division of the stitch will not restore atrioventricular conduction. Among four patients in this group who suffered this accident, three died.

Results

The results of attempts at surgical closure in 100 consecutive atrial septal defects by the digitally guided external suture method are given below.

Ostium Primum Defects. There were 17 patients with "ostium primum" or "endo-

TABLE 1.—*Interatrial Septal Defects*

Total	100
Ostium secundum	83
Ostium primum	17

TABLE 2.—*Ostium Primum Defects*

	Cases, No.
Total	17
Preoperative catheterization	17
Shunts calculated	9
Average L-R shunt....4.5 L./min.	
Average R-L shunt....0.3 L./min.	
Pulmonary hypertension	14
Operative deaths	12
Deaths in patients with hypertension	10
Minimal	3
Moderate	2
Marked	5

cardial cushion" defects. In two of them anomalous pulmonary venous drainage existed, and in none was mitral stenosis found. One of these patients also had a small septum secundum defect. The amount of shunt was calculated in nine patients. The average left-to-right flow was 4.5 liters per minute. The average right-to-left flow was 0.3 liters per minute. In one, the shunt was "balanced."

Pulmonary hypertension was present in 14 of the 17 patients. It was minimal in three, moderate in four, and marked in seven.

Only 5 of these 17 patients survived operation, a survival rate of only 29%. There seemed to be no significant correlation in this small group between the levels of pulmonary arterial pressure, transatrial flow, and operative survival (Tables 1 and 2).

The deaths appeared to be related chiefly to injury of the common atrioventricular conduction bundle (three deaths in four cases) and to postoperative circulatory failure. For the most part, this failure was related to a technical inability to close the communication due either to difficulty in reaching the deep lower aspect of the defect or to "tearing-out" of these marginal sutures after they had been placed.

Ostium Secundum Defects: Eighty-three patients in this series presented ostium secundum defects. The magnitude of the left-to-right shunt was calculated in 60 patients and averaged 6.5 liters per minute. Thirteen of the eighty-three died following surgery, a mortality of 15.6%. Nine presented a "balanced shunt" (less than 1.5 liters left-to-right shunt with a calculable right-to-left shunt, however small). Eight of the nine died following operation and were included in the over-all mortality rate. If the patients with balanced shunts had been excluded from surgery (as is our present practice), the operative mortality in patients with septum secundum defects would have been reduced to 5.4% (Tables 3 and 4).

TABLE 3.—*Ostium Secundum Defects*

	Cases, No.
Total	83
Shunts calculated preoperatively	60
Average L-R shunt....6.5 L./min.	
Average R-L shunt....0.16 L./min.	

TABLE 4.—*Defects of the Ostium Secundum in Eighty-Three Cases*

Type of Shunt	Cases, No.	Operative Deaths	Operative Mortality, %
Balanced shunt	9	8	89
Left-to-right shunt			
Greater than 1.5 L./min.	74	4	5.4

	Cases, No.
Postoperative catheterization	40
Shunt abolished	38
Minor residual shunt	2
Defect closed	95%

There were 16 patients with associated anomalous drainage of the right pulmonary veins into either the right atrium or one of the venae cavae. One of these patients had both mitral stenosis and an anomalous right pulmonary vein. Thus, 19% presented coexisting anomalous pulmonary venous drainage. In most of these patients the septal defect was of the posterior type. Three of the defects were high ones (cephalad) and the anomalous drainage was into the superior vena cava (Table 5).

TABLE 5.—*Ostium Secundum Defects*

	Cases, No.
1. Uncomplicated (by other cardiac lesion)	59
2. Associated anomalous pulmonary venous drainage	15
3. Associated mitral stenosis	8
4. Associated anomalous pulmonary veins and mitral stenosis	1
Total	83

There were nine patients with associated mitral stenosis, an incidence of Lutembacher's syndrome of 11%. The valvular lesion was corrected simultaneously with the septal one in each case. There was one death in this group (a patient with a balanced shunt).

Right heart catheterization has been carried out in 81 of the 83 patients preoperatively and, up to this date, in 40 patients postoperatively.

Preoperatively, some degree of pulmonary hypertension was present in 64% of this group. This was classified as minimal hypertension (30-40 mm. Hg) in 32%, moderate hypertension (41-70 mm. Hg) in 11%, and severe hypertension (above 70 mm. Hg) in 21%.

Among the 70 patients who survived operation, the preoperative left-to-right shunt was calculated in 47 and averaged 7.3 liters per minute. In the 10 with marked hypertension, the average left-to-right shunt was 4 liters per minute.

Among the 13 patients who died subsequent to surgery, the shunts were calculated in 10. The average left-to-right shunt was 2.7 liters per minute, and the average right-to-left shunt was 0.4 liters per minute. If two patients in this group with left-to-right flows, respectively, of 14.8 and 4.5 liters per minute (and with normal pulmonary arterial pressures) are excluded, the average left-to-right flow in the remaining nine was less 1.3 liters per minute. These then may be considered to have had "balanced" shunts at the time of operation and are the ones referred to previously (Table 6).

Pulmonary hypertension existed preoperatively in 12 of the patients who died. It was minimal in four, moderate in one, and marked in seven (Table 6).

Among the 70 patients surviving surgery for ostium secundum defects, 40 have been studied physiologically since operation. The shunt was found to have been abolished and the defect presumably completely closed in 38. In two, a residual, but smaller, shunt persisted. Both patients since have been reoperated upon. One died (and is included among the thirteen deaths in this group); the other has not yet been recatheterized (Table 4).

TABLE 6.—*Ostium Secundum Defects, Operative Deaths*

	Cases, No.
Total	13*
Pulmonary hypertension	12
Minimal	4(33.3)†
Moderate	1(8.3)
Marked	7(58.4)
Shunts calculated	11
L-R shunt, av.	2.7 L./min.
R-L shunt, av.	0.4 L./min.

*Two patients of 13 who died had L-R shunts. Excluding two the average L-R shunt was 1.5 L./min. or less.
†Per cent values are given in parentheses.

Comment

Clinically the response among the survivors of surgery has been most gratifying. Relief of shortness of breath and disappearance of signs of heart failure have been striking.

As previously reported by two of us (H. G. and D. D.),[28] after surgery one may expect a reduction in heart size (by x-ray) in 75% of the cases, reduction in the size of the pulmonary artery in 57%, and a decrease in the pulmonary vascular markings in 78%.

In selecting patients for surgery, four factors stand out significantly:

(1) The ostium primum type of defect at the present time does not seem to be amenable to surgical correction by the closed external suture method (atrioseptopexy). Seventy-one per cent of these patients (with "endocardial cushion defects") failed to survive surgery when the closed technique was applied as described. Similarly discouraging results have been experienced by Gross[5] (using the "well" or semiclosed technique) and Lewis,[25] using an open technique and hypothermia in operating upon defects of the septum primum.

(2) The presence or absence and the degree of pulmonary hypertension, and (3) the direction and amount of shunting of blood through the defect constitute a complex but most important interrelation of

TABLE 7.—*Interatrial Septal Defects*

Characteristics of the ideal case	
1. Defects of septum secundum type	
2. Left-to-right shunt greater than 1.5 L./min.	
3. Absent or minimal pulmonary hypertension	
Results in our first 74 patients thus classified, %	
Survivals	94.6
Defects closed	95.0

indications and deterrents which must be evaluated individually in every patient.

A very high mortality (eight out of nine) was experienced with those patients who presented a "balanced shunt." While the single survivor reports considerable subjective improvement, we are unable to confirm this either objectively or physiologically. Her pulmonary arterial pressure, which was 98/30 (55 mean pressure) preoperatively, remains unchanged postoperatively.

(4) The fourth factor concerned with the operative mortality is the technical proficiency of the operator. Three of the deaths in our series were clearly due to surgical errors which should be avoidable in the future.

Less prominent among the causes of mortality has been the anticipated and originally feared possibility of pulmonary or systemic embolism. There has been only one death in this series from this cause (multiple pulmonary embolization).

Patients who are properly selected for atrioseptopexy may expect a survival rate of 94.6% (in this series) and complete abolition of the shunt in nearly every instance (95%) (Table 7).

Summary and Conclusions

One hundred consecutive cases of atrial septal defect subjected to an attempt at surgical correction by atrioseptopexy (internally guided but external suture technique) have been reviewed.

Because of the very considerable risks which presently are associated with the employment of either of the two methods for open cardiac surgery (hypothermia or the extracorporeal circulation), it is felt that the closure of atrial septal defects of the secundum type by atrioseptopexy continues to be the simplest, safest, and clinically most satisfactory method of treatment available at present.

The use of the closed suture method is not justified for defects of the ostium primum type.

Patients who present right-to-left or "balanced" shunts due to increased pulmonary vascular resistance should not be subjected to operation for closure of their defects, which by this time will have attained a partially "compensatory" status. Perhaps further advances in our understanding of the altered physiology and the pathology of these cases will lead to a different conclusion.

The coexistence of anomalous drainage of the right pulmonary veins or of mitral stenosis does not increase the operative risks providing the additional lesion is corrected simultaneously.

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Cardiac Arrest—The Most Important Disaster in the Operating Room

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The Challenge

It is undeniable that thousands of patients, young and old, lose their lives each year throughout the country, because their hearts stop beating suddenly in the operating room during anesthesia and operation. This disaster will be discussed under the following headings:

I. What is cardiac arrest?
II. How often does cardiac arrest occur?
III. In what type of patients and at what ages does cardiac arrest occur?
IV. In what types of operations does cardiac arrest occur?
V. When and where does cardiac arrest occur?
VI. What are the causes of cardiac arrest?
VII. With what anesthetic agents does cardiac arrest occur?
VIII. How can cardiac arrest be prevented?
  (*a*) By the internist
  (*b*) By the anesthetist
  (*c*) By the surgeon
IX. What is the best program for early detection of cardiac arrest?
X. What is the treatment of cardiac arrest?
XI. What is the prognosis of cardiac arrest?

I. What is Cardiac Arrest?—The term "cardiac arrest," as employed by the surgeon, requires definition. Everyone who dies undergoes "cardiac arrest." Moreover, a number of patients die in operating rooms more or less quickly for obvious reasons such as surgical shock; sudden, excessive blood loss, or obviously difficult, prolonged anesthesia. However, we are discussing the sudden, usually unexpected, complete cessation of heart action occurring in the operating room in the anesthetized patient. It is desirable to distinguish between cardiac arrest occurring during an operation on the heart or great vessels and the cardiac arrest which may occur during thoracentesis, appendectomy, laryngoscopy, or circumcision. Death of the patient is equally tragic, but the mechanism of heart arrest may be quite different. Early recognition and effective treatment varies widely between these two groups of cases.

The heart is a very durable organ. It is obviously designed to beat incessantly. As Potts states, the heart "is the most efficient, self-sustained pump in the world."[1] Only the lungs and brain centers can compare in the necessity of its continuous performance. It suffers far less from brief periods of oxygen deprivation than do the brain or liver cells. It may be stated dogmatically that the heart never ceases to beat except for adequate cause. Yet it may be difficult or impossible to assign cause for the occurrence of cardiac arrest in a number of patients. It is frequently possible to restore regular heart beat, at least temporarily, even though the patient may die subsequently in a few hours or several days, because of irreparable damage to the medullary centers from lack of oxygen.

II. How Often Does Cardiac Arrest Occur?—An exact answer cannot be given. It seems probable that throughout the country there are from 3000 to 10,000 cases a year. The exact number of deaths from cardiac arrest in Massachusetts last year is not obtainable. Dr. Paul Zoll[2] estimates that approximately 100 and not more than 125 cardiac arrests occurred in this state last year. Beecher and Todd, from their comprehensive survey based upon reports from 10 participating, teaching hospitals,[3] make an estimate of 1 in 3000 anesthetized pa-

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tients. This incidence ranges from once in 1000 elderly or poor-risk patients to once in 5000 young anesthetized patients in whom minimal or no physical impairment is apparent. It must be acknowledged that a great many instances of cardiac arrest in the operating room are not recorded. It is possible that this disaster occurs even oftener in the very many smaller, nonteaching hospitals throughout the state in which the number of beds and the number of yearly operations is much larger than in the relatively few teaching hospitals in the larger centers. It is probable that many cases of cardiac arrest are not specified as such on death certificates.

It has been suggested that cardiac arrest should be regarded as a public health menace since it is fairly frequent, usually preventable, and often fatal. It is gratifying that the Massachusetts Heart Association has recognized the frequency and urgency of this condition and is distributing basic instruction sheets on its prevention and treatment. It is to be hoped that all physicians who anesthetize and who operate will secure this information. From a medicolegal standpoint, it would seem probable that in the future an anesthetist or a surgeon would be vulnerable to lawsuit if he had had the misfortune to encounter a case of cardiac arrest in the operating room in which the currently recommended standard procedure for resuscitation had not been carried out.

III. In What Patients and at What Ages Does Cardiac Arrest Occur?—Cardiac arrest may occur in the anesthetized patient at any age; with any anesthetic agent, including local anesthesia, and during any operation, whether major or minor.

Age of Patient: In the largest series, arrest was most frequent in the first decade of life.[4] In a recent report, it occurred more often in elderly patients.[5] It is understandable that arrest has been commoner in young patients in recent years, because so many congenital defects of the heart are being operated upon. In general, it is probable that this complication occurs more frequently in the older age group of patients, in whom various degenerative diseases affecting neuromuscular conductivity in the heart, or adequate pulmonary ventilation, would be present more commonly.

It is important to stress that sudden cessation of heart action and subsequent death, if resuscitation is not attempted and successful, occurs in young children during tonsillectomy, in college students during laryngoscopy, in young adults having such routine operations as appendectomy, Cesarean section, or circumcision. No doctor can assume that he can ignore the possibility of this disaster in his patient because the patient is young or because his operative procedure is a routine or minor one, far removed from the throat, neck, or mediastinum. Cardiac arrest has occurred during the extraction of a single tooth under thiopental (Pentothal) anesthesia. This tragedy can happen to a dentist, oral surgeon, nose and throat specialist, general surgeon, urologist, gynecologist, or orthopedic surgeon.

IV. During What Operations Does Cardiac Arrest Occur?—It occurs more commonly in operations on the throat, neck, mediastinum, and heart. Heart operations naturally stand in first place. Even rotation or displacement of the heart during an operation on adjacent organs may cause arrest of heart action. It has happened frequently during tonsillectomy. It is not uncommon during radical neck dissection or thyroid operations during which the carotid body at the bifurcation of the common carotid artery, or the vagus nerve, may be manipulated. The presence of the carotid body must not be overlooked by the surgeon operating in the neck. In the occasional patient, procaine hydrochloride (Novocain) injection in the region of the carotid bifurcation may be desirable to suppress inhibition of heart action by vagal stimuli from the carotid body.

Operations in the upper mediastinum and around the hilum of the lungs or on the thoracic aorta may be provocative. Arrest of the heart may be stimulated by forcible spreading of a chest wall retractor or vigorous traction on epigastric organs. It must

be recognized that, in varying degree, sensory impulses from almost any part of the body are capable of influencing the vagus nerve. From experiments done as students in the physiological laboratory, it may be recalled that such techniques as eyeball pressure, the Valsalva procedure, induced vomiting, or pressure of the carotid bifurcation can cause slowing of the pulse by stimulation of the vagus nerve.

V. When and Where Does Cardiac Arrest Occur?—Ninety per cent of these accidents occur in the operating room in anesthetized patients. Cardiac arrest apparently happens more often at the beginning or at the end of operations. Vagal stimulation during initial intubation or during extubation and tracheal toilet at the end of operation is more comprehensible, but in a number of instances this disaster is first noticed as the surgeon is about to make his incision or the position of the patient has just been changed.

But heart beat has ceased suddenly in a variety of circumstances. It has occurred in the x-ray department during cardiac catheterization. It takes place in the recovery room, at times after an uneventful operation. It has happened during cystoscopy in a physician's office. Of course, it is difficult to be certain of the exact diagnosis under these circumstances. The results of a massive pulmonary embolus or coronary thrombosis may closely resemble arrest. A recent cartoon depicts the occurrence of cardiac arrest on the golf course, with immediate attempt at cardiac massage.[6] Beck predicts that nonmedical attendants will be taught to open the chest and pump the heart, in the years to come.

VI. What Are The Causes of Cardiac Arrest?

A. Decreased Oxygen Supply to the Heart (hypoxia).

B. Increased Amount of Carbon Dioxide in the Lungs, and Hence in the Circulation (Hypercapnea). This is respiratory acidosis.

C. Electrolyte Imbalance.

D. Direct or Reflex Stimulation of the Vagus Nerve.

E. Unknown. Certainly in a number of cases, no apparent cause can be assigned.

A. Hypoxia: The primary concern of the anesthetist, particularly in the poor-risk patient, must be to avoid any lack of oxygen or excess accumulation of carbon dioxide. Lack of oxygen will occur rarely because there is insufficient oxygen in the inspired gas mixture. However, as Saklad has emphasized, insufficient oxygen may be available to the myocardium because of a wide variety of disorders.[7] A patent airway, adequate exchange of alveolar air, adequate red blood cells to carry the oxygen, adequate myocardium to propel the transported oxygen, adequate arteries in the myocardium to convey it, and adequate cell utilization are all necessary. For example, acute myocardial ischemia with subsequent arrest could result from failure to aspire bronchial secretions, sudden massive hemorrhage during operation, or pressure by the surgeon's hand on a coronary blood vessel, particularly the left descending branch.

B. Hypercapnea: The constant goal of the anesthetist is to ensure adequate ventilation. This involves the supply of enough oxygen and also the adequate elimination of expired carbon dioxide. Regulation of oxygen supply is rarely overlooked. Much less attention has been focused upon the second, imperative pulmonary function, the elimination of carbon dioxide. Cyanosis is an easily recognized sign of failure of the first function. However, detection of failure of the second function is much more difficult and may even be masked by the modern, closed rebreathing circuit. Incomplete expiration of carbon dioxide in lung alveoli may occur during a prolonged operation and in the presence of alveolar hypoventilation. Such an inadequate ventilation of alveolar air in the periphery of the lung is responsible for the accumulation of excessive carbon dioxide (respiratory acidosis). In this manner, secondary acidosis of the circulating blood may result, with reduction of alkali reserve. The blood pH may be reduced from the normal of 7.35 to a level of 7.1, or even

lower. Cardiac irritability with EKG changes and the threat of cardiac arrest or ventricular fibrillation have been greatly lessened in recent years by wider recognition of the continuous need for adequate alveolar ventilation. Such progressive respiratory acidosis occurring during thoracic operations because of alveolar hypoventilation, has been pointed out.[8,9]

In addition to respiratory acidosis, metabolic acidosis, with increased sensitivity of the conduction system, may result in a patient because of prolonged sepsis, unregulated diabetes, or protracted anesthesia.

C. Electrolyte Imbalance: The chemical regulation of heart action is expressed by the equation

$$K=\frac{\text{calcium-sodium-magnesium}}{\text{potassium-hydrogen ion concentration}}$$

where

K=myocardial contractility

It has been known experimentally for more than 35 years that intravenous potassium chloride can cause standstill of the heart and that calcium chloride given thereafter will bring about resumption of normal rhythm.[10] As early as 1929, Hooker suggested the use of potassium chloride to stop a fibrillating heart and calcium chloride thereafter, to restart normal heart beat. Thirty years later, Melrose [11] suggested the injection of potassium chloride into the heart in the region of the sinoauricular node to produce complete arrest for open heart surgery. Both the sodium and the calcium ion stimulate myocardial contraction. Molar sodium lactate increases cardiac rhythmicity and may counteract cardiac inhibition by hyperpotassemia.[12] An excess of calcium causes standstill in extreme systole (calcium rigor). It has recently been suspected that some cases of cardiac arrest may have resulted from multiple transfusions in which the citrate in the transfusion united with the available, circulating calcium ion to result in a calcium deficiency. By contrast, cardiac surgeons are obtaining a dry, stopped heart by the combination of potassium citrate injection at the root of the aorta together with the use of the extracorporeal heart-lung machine. This is deliberate, elective cardiac arrest.[13] Such knowledge of the chemical regulation of heart action emphasizes both the need of restoration of normal electrolyte balance prior to surgery and the useful role of agents such as calcium chloride in the operative management of the absent or sluggish heart beat.

D. Direct or Reflex Stimulation of the Vagus Nerve: The prominent role of the vagus nerve appears to be undeniable. Physiologist call attention to the fact that the vagus nerve is more influential in the regulation of heart beat than are the sympathetic nerves. Moreover, there is individual variation in the degree of reactivity of the vagus nerve to such stimuli as eyeball pressure or pressure on the carotid sinus. Sloan demonstrated clearly that vagal inhibition of heart action is accentuated in the presence of diminished oxygen or increased accumulation of carbon dioxide.[14] Impulses are dispatched to the vagus nerve both by the cardiac center in the medulla and by the carotid body in the neck. Apparently, a wide range of afferent nerve fibers from various parts of the body are capable of influencing vagal activity. The etiological role of marked preoperative apprehension is difficult to evaluate, but presumably in such instances death may occur from cardiac arrest due to stoppage of the heart by excessive vagal restraint. Certainly, many experienced surgeons have been reluctant to perform elective surgery for a patient who expressed the strong conviction of impending death if operation were performed.

E. Unknown Causes: From the literature and our experience with 12 cases at the Salem Hospital, it may be concluded that it is not possible to assign a logical cause in some cases of cardiac arrest.[15]

VII. With What Anesthetic Agents Does Cardiac Arrest Occur?—Cardiac arrest may occur during anesthesia secured with any agent, including local anesthesia. Ether, cyclopropane, and trichloroethylene are organic

hydrocarbon drugs capable of harmful depression of function in the myocardium, conducting system, and autonomic nervous system. Ether may cause an increased amount of circulating epinephrine.[16] Cyclopropane is a powerful respiratory depressant. Acidosis may occur frequently when cyclopropane is employed, even with assisted respiration. By contrast, nitrous oxide has specific depressing action on the central nervous system without known harmful effects either on the myocardium or the conduction system in the heart. There is increasing enthusiasm for operation under light plane anesthesia with nitrous oxide and the muscle relaxants.[17] However, it is obvious that the selection of a particular anesthetic agent is less important than the skill of the particular anesthetist in securing adequate respiratory and circulatory function.

VIII. How Can Cardiac Arrest Be Prevented?—It cannot be emphasized too strongly that cardiac arrest is a preventable disaster. Much more attention should be devoted by internist, anesthetist, and surgeon to the technique of prevention than to the technique of resuscitation.

A. Prevention by the Internist: 1. Restoration of normal blood volume prior to surgery. Hypotension with secondary hypoxia of medulla and heart muscle occurs more quickly and more often and is much more difficult to regulate in patients undergoing major surgery in whom adequate blood volume has not been restored prior to operation. In most patients, deficiency of blood volume may be obvious or suspected because of a history of weight loss, prolonged fever, obvious malnutrition, or vomiting, in addition to the standard laboratory determinations for red blood cells, hemoglobin, and hematocrit value. However, significant reduction in blood volume may be present, particularly in patients with carcinoma, in whom the history and the usual laboratory values are inconclusive. In such patients the determination of blood volume, as by the Evans dye test or isotope dilution techniques, may pay a rich dividend. Nor should the surgeon assume that the required blood given rapidly in the operating room at the start of operation is as beneficial as a similar amount of blood given prior to operation. The possible danger in reduction of available calcium ions in the circulation, by the administration of multiple citrate transfusions, has already been mentioned. Attention should be called to the fact that banked blood may also contain an excessive amount of potassium.

2. Electrolyte balance. Considerable interest is currently devoted to artificial, chemical regulation of the heart beat by the surgeon at the time of operation, which serves to emphasize the desirability of obtaining normal electrolyte values prior to operation, if possible. This is of particular importance in the chronically ill patient who has been unable to eat or has suffered loss of large amounts of gastrointestinal fluids.

3. The recognition and adequate treatment of depleted cardiac or pulmonary reserves. Additional bed rest may be required for a patient who shows any degree of heart failure on admission to the hospital. Regulation of abnormal heart beat by digitalis or quinidine may be indicated. However, digitalis must not be given routinely to elderly patients, since it slows down conduction time and might play a causative role in the arrest of heart action. A patient with a diminished pulmonary reserve because of chronic disorders such as bronchitis, asthma, or emphysema may require a longer preoperative period of bed rest. Electrocardiograms and x-rays of the chest should be obtained more often, particularly in the older age group of patients who are being prepared for major surgery such as resection of the stomach or colon.

B. Prevention by the Anesthetist: 1. Careful selection of the anesthetic agent best suited to the individual patient and his proposed operation. As mentioned, there is current enthusiasm for operation under "light plane" anesthesia obtained with nitrous oxide and oxygen together with the muscle relaxants. It is alleged that harmful EKG

changes, indicative of cardiac irritability or arrhythmia, are encountered much less often with such an anesthetic combination. It must be acknowledged that such "light plane" anesthesia may be safe and adequate for older patients but may not provide sufficient muscle relaxation in younger patients. Moreover, the number of deaths in the operating room during the induction of such anesthesia has been reported as being five times greater when the muscle relaxant drugs were employed.[8] Nevertheless, Beecher comments that the muscle relaxants should not, therefore, be abandoned.

2. Adequate level of preoperative sedation. Deep sedation may interfere with the normal protective reflexes; sedation which is too light is certainly undesirable, particularly in the apprehensive patient.

3. The use of atropine. Atropine blocks the release of acetylcholine by the vagus nerve and thus prevents excessive slowing of the heart rate. Some have argued that an excessive, even dangerous, dose of atropine would be required to block all vagal impulses. Others allege that cardiac arrest in the operating room occurred less frequently in former years because preoperative atropine had been employed more commonly. Some anesthetists prefer to use scopolamine because of its sedative effect in addition to its atropine-like restriction of tracheal secretions.

4. Gradual, careful induction. The anesthetist must resist any impatience for rapid induction on the part of the surgeon. Cardiac arrest has often occurred just at the time of induction. Various provocative factors may be active. The apprehensive patient, perhaps lightly sedated, may secrete more epinephrine just at this time. Hypoxia from irregular, inadequate respirations occurs more often at the time of induction. Laryngospasm may be provoked by thiopental or the mechanical trauma of tracheal intubation. Without question, intubation of the larynx causes vagal stimulation. Cardiac arrest occurring just as the endotracheal tube is inserted may result from inadequate sedation, hasty or forcible intubation, or a brief period of oxygen lack. It is important to emphasize that the single anesthetist cannot monitor heart action continuously just at the time of tracheal intubation. It is probably desirable to place the responsibility for continuous observation of the carotid pulse on a second person, or a cardiac monitor, during this brief but important period.

5. An adequate airway. A faulty airway is one of the commonest causes of inadequate supply of oxygen. The anesthetist must be alert to the occasional need for preliminary aspiration of stomach contents or the presence of an inlying nasogastric tube on suction. In addition, it is obvious that periodic aspiration of tracheal and pharyngeal secretions is mandatory.

6. Adequate oxygen intake. The required amount of oxygen to be administered will vary according to the operation and the need of the patient. An inadequate supply of oxygen may be manifested by a rising pulse and increasing blood pressure because of increased release of epinephrine. Advocates of the nitrous oxide-oxygen anesthesia with muscle relaxants emphasize the generous amount of oxygen which may be administered. So-called "assisted respiration" by the anesthetist is more commonly required in the elderly, poor-risk patient or during prolonged operation, because it is suspected that there is incomplete exchange of alveolar air.

7. Excessive carbon dioxide accumulation (hypercapnea). Increasing attention is being paid by anesthetists to the chemical regulation of heart beat and the adequate respiratory exchange. The carotid sinus in the neck and the cardiac center in the medulla are both sensitive to oxygen lack and carbon dioxide excess. The heart rate is increased by slight oxygen lack or carbon dioxide excess, but severe oxygen deficiency or marked increase in carbon dioxide accumulation in the alveoli or secondarily in circulating blood cause distinct slowing of the heart or actual heart block.[18] Lesses has demonstrated actual or relative acidosis in psychiatric patients subjected to shock therapy, in whom

the blood pH was either significantly lowered or actually converted to the acid side of neutrality (6.8).[19] This important role of unexpired carbon dioxide because of inadequate alveolar ventilation has been emphasized only in recent years. This situation obtains particularly in older patients, during prolonged anesthesia, or in association with preexisting respiratory deficiency such as marked emphysema.

Hence, it is not surprising to observe the increasing interest shown in artificial ventilation as by the Jefferson Respirator or by the Autoanestheton.[20,21] These mechanical breathing machines are designed to respond automatically to the need for greater oxygen supply or incomplete expiration of carbon dioxide, on the basis of periodic determination of the oxygen-carbon dioxide content of the ventilated air.

8. Continuous, close observation of the cardiac rate and rhythm. Cardiac arrest may actually be averted, in occasional cases, by the withdrawal of all anesthesia, whenever such changes as bradycardia or rapid runs of ectopic ventricular beat are observed. Cardiac arrest may be averted at times by cardiac stimulation when the threat of failing circulation exists. For example, administration of levarterenol bitartrate (Levophed) or calcium chloride or more rapid transfusion of blood may provide additional needed support for the heart and vascular system, at a critical period.

9. The removal of the endotracheal tube. Cardiac arrest has commonly occurred both at the time of insertion and on removal of an endotracheal tube. A diminished oxygen supply is probably a factor. Severe laryngospasm may ensue as such a tube is withdrawn. An earlier, initial dose of atropine may have become dissipated. The administration of an additional dose of atropine, perhaps intravenously (1/100 grain [about 0.6 mg.]), may be desirable a few minutes prior to extubation. Some anesthetists favor the instillation of 2 cc. of topical anesthetic through the trachea prior to removal of such a tube. Subsequent coughing in the lightly anesthetized patient results in a spraying of the injected solution over the vocal cord.

10. Hyperventilation at the end of operation. Vigorous ventilation with pure oxygen has been commonly practiced by the anesthetist at the close of an operation. However, there is some danger in this practice. The maintained excess of alveolar carbon dioxide during operation tends to produce vagoconstriction because of the secondary increase of CO_2 in the circulation. But a sudden fall in blood pressure may result when this excess of carbon dioxide is rapidly dissipated from the alveoli and the circulation by hyperventilation with pure oxygen. In animal experiments, 80% of dogs have died from ventricular fibrillation and cardiac arrest when the animals were rapidly ventilated with room air after a prolonged period of breathing an excess of carbon dioxide (30%-40%).[22] Both the accumulation of carbon dioxide in the alveoli and the rapid correction of retained carbon dioxide must be avoided to eliminate this sudden dropping of blood pressure which may occur in the immediate postoperative period during recovery from such respiratory acidosis. This mechanism has been thought to be the explanation of so-called "cyclopropane shock." It has been observed, for example, when the patient is moved from the operating table to a stretcher at the close of operation.

A second hazard must inspire caution in forced ventilation with pure oxygen at the end of operation. A dangerous period of apnea may result. Carbon dioxide has a narcotizing effect on the medullary centers. Hence, a complete and dangerous cessation of respiration may occur when the patient is diligently ventilated with pure oxygen. The circulation may already contain an adequate amount of oxygen. However, the respiratory center, partially narcotized by a long period of carbon dioxide excess, may not then respond to the stimulus of pure oxygen. It is apparent that the anesthetist must exercise some caution about routine hyperventilation with oxygen only, particu-

larly at the close of a long operation and in patients with limited respiratory function.

11. The proper level of anesthesia for the individual patient. It is axiomatic that deeper anesthesia is more harmful to the patient. In the majority of operations, neither prolonged nor deep anesthesia is required. The surgeon operating in the thorax has less need of deep muscle relaxation. The surgeon operating on the abdomen may be inclined to request a deeper level of anesthesia during such operations as colectomy or gastrectomy. However, the anesthetist must strive for a level of anesthesia which is primarily the safest for his patient and secondarily provides a degree of muscle relaxation and quiet breathing which permits the surgeon to perform his operation expeditiously.

12. Maintenance of adequate blood volume. The anesthetist must be responsible for quantitative replacement of blood loss as it occurs. In many cases he is more qualified than the surgeon to observe total blood loss, not only the obvious bleeding in the wound but also the degree of blood loss reflected in the sponges and packs retrieved from the operating table.

C. Prevention by the Surgeon: 1. The position of the patient. During thoracotomy, it is apparent that ventilation is handicapped somewhat when the patient's body is resting upon the functioning side of the chest. Overholt has proposed the prone position which, of course, permits a freer excursion of the thoracic cage on the unoperated on side. It has been found that less change in the pH of the blood is observed during thoracotomy in this position.[8]

In pelvic surgery a moderate degree of Trendelenburg position is often useful. Even a marked lowering of the head end of the table may be well tolerated in a young patient in good condition. However, the surgeon must not require a similar degree of Trendelenburg position for all pelvic surgery regardless of the age and condition of the patient. Without question, adequate aeration may be seriously handicapped in some patients.

2. Surgical technique. The surgeon must be cautious about displacement or traction on organs when operating in the vicinity of the heart and the great vessels. He should beware of excessive stimulus to the vagus nerve, either directly, in operations in the upper mediastinum, or indirectly, during operations on the neck, chest, or upper abdominal organs. Forcible retraction of a thoracic or epigastric incision should be avoided. Excessive traction on mediastinal or epigastric organs is undesirable. The operation should be conducted with reasonable speed, since acidosis tends to be cumulative. The surgeon must accept some responsibility for maintenance of adequate blood volume and blood pressure, together with the anesthetist. The surgeon should remember that cardiac arrest may be provoked during operations on the heart or great vessels, either by sudden massive blood loss or temporary occlusion of coronary blood flow by pressure on the heart.

IX. What Is the Best Program for Early Detection of Cardiac Arrest?—It should be reiterated that the earliest possible detection of arrest of heart action is more important than the exact technique of subsequent treatment. The life of the patient hinges upon early detection and immediate treatment. The onset of cardiac arrest may be detected by the anesthetist, the surgeon, or a cardiac monitor. These monitors give immediate indication that heart beat has ceased. It seems very probable that these mechanical guardians will be used more frequently in the future, particularly in elderly or poor-risk patients. One of the recent and most satisfactory monitors records a visual and audible signal of each heart beat.[23] It will actually ring a bell with the onset of cardiac standstill or fibrillation. It can be regulated to provide an immediate electrical shock to the stopped heart. Less satisfactory monitors provide audible or visible recording of the heart beat or pulse at the precordium or at the wrist. The oscilloscope is a continuous

visible electrocardiogram. It should be remembered that even after regular heart beat has ceased a bizarre electrocardiogram may still be recorded for short intervals.

1. The Anesthetist. Without question, the alert anesthetist is the best and most practical monitor of heart action. It may be difficult for the anesthetist to keep his finger continuously or the carotid pulse during induction of anesthesia. His hand may be completely employed with intubation of an endotracheal tube. Unfortunately, cardiac arrest may occur just at this time. Moreover, the anesthetist may be required to adjust the intravenous solution or to arrange the lighting on the operative field. Such varied tasks may interrupt his continuous surveillance of the patient's pulse and color for only a few seconds. However, the attention of the anesthetist must not be diverted to these secondary tasks, particularly in poor-risk patients. During prolonged operations it would seem desirable to replace the initial anesthetist, since it is obviously difficult to maintain continuous diligence for a number of hours, particularly when no change is apparent in the patient's condition. Moreover, it may be desirable to obtain another physician or nurse to observe the patient's pulse during several vital periods in which an endotracheal tube is being inserted or removed, the position of the patient has to be changed, or an intravenous needle has to be adjusted. Perhaps it should be mentioned that his continuous responsibility does not permit the anesthetist to read his mail, or the daily paper, or a current medical journal. Doubtless all anesthetists agree with the principle of undivided attention to the unconscious patient, but, as a practical observation, the attention of the anesthetist may be diverted briefly by a number of activities which are not as important to the welfare of the patient.

2. The Surgeon. The surgeon is not a good monitor of heart action unless he is operating upon the heart or adjacent great vessels. He may be engaged in a prolonged operation in a relatively bloodless field in which too much valuable time might elapse before he became aware of color changes in the tissue or the complete absence of arterial bleeding.

3. The cardiac monitor. It seems probable that such instruments will become increasingly popular. It is impossible to visualize their future at this time. They are expensive. It would be necessary to employ a monitor in every anesthetized patient in order to detect every cardiac arrest just as soon as it occurs. However, the cardiac monitor is one solution to two great problems with this disaster: (1) the earliest possible detection that the heart has stopped and (2) immediate electrical stimulation of the inert heart prior to the onset of myocardial anoxia, without the hazard of thoracotomy in a desperately sick patient.

X. What Is The Treatment Of Cardiac Arrest?—Two goals of treatment should be stressed: (1) restoration of the oxygen system and (2) restoration of the normal heart beat.

This is the most urgent emergency in the operating room, surpassing even massive hemorrhage. Control of hemorrhage can often be accomplished by only one person, the surgeon. Control of cardiac arrest demands the speediest coordinated effort on the part of surgeon, anesthetist, and operating room staff. The heart is a remarkable and durable organ. In most patients, heart beat can be restored fairly readily. However, the brain cells tolerate lack of oxygen very poorly. Irreparable damage occurs after three to four minutes of oxygen lack. An even greater tragedy than death in the operating room from cardiac arrest is the recovery by diligent treatment of a decerebrate person. In Stephenson's long series of collected cases (1200), 8 patients survived who were decerebrate thereafter. One such tragic survival of a previous college student has occurred in our area.

It is pertinent to discuss briefly the treatment of cardiac arrest occurring elsewhere than in the operating room. In the report by Stephenson it was stated that resuscita-

tion outside the operating room had been successful in 17% of the cases. Such resuscitation may be feasible in a recovery room which is adjacent to the operating suite, or even elsewhere in the hospital if minimal facilities are available such as an oxygen tank, face mask, airway, and knife. Beck has recently reported (June, 1956) the "death" of a physician dressed in street clothes who was leaving the hospital and in whom successful manual systole and electrical defibrillation were carried out.[24] Another very recent report cites a similar survival in the emergency room, of a patient in ventricular fibrillation secondary to coronary occlusion.[25] Beck has speculated that in the year 2000 A. D. the practice of cardiology will embrace the possibility of chests being opened and hearts pumped by hand right on the golf course. It is encouraging to learn of these isolated successes, but, as a practical program, it is strongly suggested that most hospitals should restrict attempts at cardiac resuscitation to those cases of cardiac arrest occurring in or nearby the operating room.

Courage: In this very urgent situation, the anesthetist must have the courage to tell the surgeon immediately that the heart has stopped when he first detects cessation of pulse. The surgeon must have the courage to perform an immediate thoracotomy and manual systole, if 30 seconds of preliminary effort are unavailing.

Dont's in cardiac arrest:

1. DON'T call for a stethoscope in order to listen for heart beat.
2. DON'T take time to change the blood pressure cuff from one arm to the other.
3. DON'T delay to obtain an electrocardiogram or medical consultant.
4. DON'T postpone thoracotomy while someone is obtaining the cardiac pacemaker from another room.
5. DON'T postpone thoracotomy in the hope that the heart beat will be resumed when the anesthetist flushes the lungs with pure oxygen.
6. DON'T postpone thoracotomy for longer than 30 seconds while the precordium is thumped or the myocardium is stimulated by a long empty needle thrust through the chest wall.

There are two critical periods of time: (1) the length of time which elapses between the onset of cardiac arrest and its discovery and (2) the length of time which passes prior to the restoration of circulating oxygen by manual or spontaneous systole. The newest cardiac monitor and stimulator is advantageous in that it is capable of shortening both these important periods. Even without such a monitor the surgeon may delay very briefly prior to thoractomy, if he feels confident that the exact time of onset of cardiac arrest is known. It must be acknowledged that various measures, such as striking the chest wall forcibly, needle injection into the heart, or forced ventilation with pure oxygen, have at times been associated with the resumption of regular heart beat. However, the over-all effectiveness of any of these temporizing maneuvers cannot compare with thoracotomy and manual systole, which obviously restores a limited circulation within a few seconds.

Procedure for the surgeon:

1. If the onset of cessation of heart beat has been detected immediately, it is perhaps reasonable to pound the precordium forcibly and even thrust a long empty lumbar puncture needle through the chest wall into the myocardium. Vasopressor drugs should not be injected. Delay for such procedures should not take longer than 25 or 30 seconds. A small sterile set of instruments for thoracotomy should be immediately available in all operating rooms.

2. Thoracotomy. Incision should be made in the fourth or fifth interspace extending from the sternum to the midaxillary line. The surgeon should not delay to obtain gloves or a sterile knife. The wound will not bleed if the heart has stopped, but, if resuscitation is successful, chest wall bleeding must be controlled later on, particularly from a divided internal mammary artery. In an adjacent hospital a patient died subsequently from continuing bleeding from a divided internal mammary artery, after regular heart beat had been restored.

3. The narrow inadequate opening in the chest wall may be widened (*a*) by dividing the costal cartilages of the fourth and fifth ribs anteriorly or (*b*) by the insertion of a 2 in. wide, Kelly abdominal retractor. Such a retractor can be inserted in the axis of the wound and the handle then rotated, which will spread the thoracotomy incision, or (*c*) by a self-retaining chest wall retractor. The wrist becomes very compressed by the adjacent ribs unless the ribs are held apart.

4. The pericardium need not be opened immediately. The heart can probably be pumped as well without opening the pericardium, and heart beat may be restored quickly. However, it is obvious that the exact condition of the heart muscle cannot be recognized unless the pericardium is opened. Therefore, after manual systole has been practiced for a short time, and if regular heart beat is not resumed, the pericardium should then be opened.

5. Manual systole. The heart should be pumped at a rate of about 40-50 times a minute. A faster rate may not permit ventricular refilling and is very tiresome. Such manual systole is capable of producing a palpable pulse in the carotid vessels in the neck and a discernible blood pressure in the neighborhood of 70 or 80. If delay in manual systole has been brief and cardiac arrest has not been caused by extensive diesase of the heart, the majority of stopped hearts respond rather quickly to this stimulus. It will be noticed that color is restored to the skin and previously widely dilated pupils may again contract.

6. The condition of the myocardium. In 85% to 90% of cases the myocardium is in a state of complete arrest. Ventricular fibrillation is encountered rarely, in the other 10%. In a very few instances a slow ineffectual heart beat is present. In one of my own cases the heart was beating feebly 20 times a minute but the clinical picture was that of complete arrest, since neither pulse nor blood pressure was present. Rarely, such a slow weak beat is encountered, but this unusual circumstance should in no way deter the institution of thoracotomy and manual systole. Such a feeble heart action will not provide the needed circulation.

7. Treatment of ventricular fibrillation. The sensation imparted to the hand by the fibrillating ventricle has been described as similar to the squirming of a cluster of worms. Immediate manual pumping of the heart must be done in order to restore coronary circulation. In some instances regular rhythm is resumed as the heart is being squeezed. The prognosis for recovery from ventricular fibrillation is of course very poor, but some examples have been reported. Defibrillation is best accomplished with the aid of an electrical defibrillator which delivers an adequate pulse current of 1.5 to 3 amperes to the fibrillating ventricles. It is desirable to have such a defibrillator available in all operating rooms.

Procedure for the Anesthetist:

1. Administer pure oxygen employing a tight-fitting face mask if an endotracheal tube is not already in place. At some later time it will be desirable to intubate the larynx.

2. Lower head end of table to promote circulation to the brain.

3. Make certain that an intravenous solution is running in an arm vein to which vasopressor drugs such as levarterenol bitartrate or phenylephrine hydrochloride (Neo-Synephrine) might be added, once circulation is restored and in order to support the blood pressure.

4. Essential drugs. The anesthetist should maintain an emergency tray in which are kept the following drugs: epinephrine 1:1000, 10% calcium chloride, procainamide hydrochloride (Pronestyl), levarterenol bitartrate, and phenylephrine hydrochloride. Initially, there may be no indication for any drug therapy. Either needle injection or epinephrine may provoke ventricular fibrillation in the ischemic, cyanotic heart. However, when the inert heart does not respond readily to manual systole, the surgeon may

elect to employ either dilute epinephrine 0.5 cc. diluted with 10 cc. of sodium chloride, or 5 cc. of 10% calcium chloride. Either agent may be injected directly into the left ventricle, although the favored site of such injection is disputed. There is diminishing enthusiasm for the use of procainamide hydrochloride. It might be employed, for example, in the rare case in which ventricular fibrillation ensued after initial resumption of regular heart beat. Procainamide hydrochloride suppresses conduction in the myocardium, and thus it may be more difficult to restore a regular heart beat after it has been administered. Vasopressor drugs might be added to the intravenous flask once circulation has been restored, in order to cause peripheral vasoconstriction.

Additional Treatment Measures:

1. Intra-aortic transfusion may be occasionally indicated, particularly if acute blood loss has occurred.

2. The distal aorta may be occluded for a brief period by hand or by clamp, if available, in order to divert oxygenated blood to the brain.

3. Brain edema results from even brief periods of cerebral anoxia. Therefore, restriction of fluids and administration of 50 cc. of serum albumin over a four- or five-minute period, every four to six hours, may be indicated in the immediate postoperative period.

XI. What is the Prognosis of Cardiac Arrest?—It is understandable that the best results occur (1) in younger patients without heart disease in whom cardiac arrest occurs as the result of reflex stimulation, (2) in patients in whom cardiac arrest has occurred as a consequence of too deep a level of anesthesia, (3) in those patients on whom the surgeon is operating in the chest or on the heart where immediate detection of arrest is possible. The statement has been made that about 50% of cases in university hospitals are now being salvaged.[5] We have had 12 such operating room accidents at the Salem Hospital. Six patients died in the operating room. Heart beat was restored in the other six patients, only two of whom survived to leave the hospital completely recovered. We have learned of eight or nine cases occurring in surrounding hospitals within the past year or two, with survival in one case. From conversation with surgeons in many of the smaller community hospitals, the impression is gained that there is a good deal of ignorance of this disaster, that there is very little preliminary standardization of procedure in the operating rooms of these hospitals, that occasional, periodic sudden deaths in the operating room are occurring, although they may not be diagnosed as cardiac arrest.

Summary

Cardiac arrest is the commonest cause of death in the operating room. The death toll from this cause throughout the country and in our own state each year is a significant one. The great majority of these deaths are preventable. There is widespread lack of knowledge about the causative mechanism and the urgent, specific treatment of the condition.

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Surgical Complications of, and Splenectomy for, Collagen Diseases

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The increasing incidence of collagen diseases and their surgical complications led us to believe that a review of some of the facts concerning these and a report of a collection of some local cases with such complications might be of interest. The frequency of occurrence of lupus erythematosus alone is now estimated to be about one-half that of rheumatic fever.[8] It is probable that an actual increase of these diseases has occurred owing to exacerbations of otherwise latent cases caused by minute quantities of drugs administered to fowl and animals and transmitted to humans through meat, eggs, and milk, since hypersensitivity and allergy, while not the sole cause, are important factors in these conditions. The increasing nervous stress and tension of modern life, leading to adrenal depletion, furthermore, may play some part. Periarteritis nodosa is now considered as one of the important diseases of adaptation. Hypoplastic and necrotic adrenal and pituitary glands have been found in this disease. Selye suggests that other collagen diseases may also belong in this category, in which a breakdown of adaptative processes to various forms of stress occurs.[21] However, the increase is also attributable to the recognition of milder cases, especially of those without the classical skin manifestations, owing to an increasing awareness of these diseases and to the use of recently introduced laboratory tests.

Collagen diseases include a group of entities in which widespread changes occur in the collagenous fibrils and interstitial ground substance of connective tissue. The pathological processes may consist of necrosis, fibrinoid degeneration, cellular proliferation, and infiltration or sclerosis. The collagenous framework, located beneath the lining endothelium of synovial and serous membranes; in joints; in the endocardium, pericardium, pleura, and peritoneum, and, especially important from the surgical standpoint, in the smaller blood vessels, is the site of injury. Duff gives an excellent description of the details of these changes.[9] For the latter types of these diseases, Zeek has suggested the appropriate term of "necrotizing angiitis."[25] Rheumatoid arthritis, rheumatic fever, systemic lupus erythematosus, periarteritis nodosa, dermatomyositis, and scleroderma are the principal collagen diseases, according to Duff.[9] O'Brien classifies rheumatoid arthritis and rheumatic fever as closely related but not strictly as collagen diseases.[16] While all may have some clinical features in common, these diseases are distinct entities, in spite of the fact that transitional forms may occur.

The etiology of this group of diseases is still obscure. Allergy has been suspected as being an important factor, but this has not been confirmed experimentally and does not explain all cases. Hydralazine, given over a prolonged period to humans, has produced a syndrome indistinguishable from acute disseminated lupus, but regression usually, but not always, has occurred on discontinuance of this drug.[21] Lesions identical to those of periarteritis nodosa have been produced experimentally in animals by repeated injections of horse serum.[20]

Attention has been called to the frequency with which dermatomyositis has been found as a precursor of malignancy.[23] More than a casual relationship apparently exists. It may be that if it can be determined what

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Fig. 1.—Pulmonary edema in a case of periarteritis nodosa, a frequent roentgenographic finding. (Reproduced with permission from Garland and Sisson,[20] *The American Journal of Surgery*, New York.)

factors in malignancy produce the changes in dermatomyositis, long before the malignancy itself is detectable by present methods, such information will prove useful in perfecting a practical test for obscure or early carcinoma.

Lupus Erythematosus

Five surgical problems were involved in the following four cases of this category: (1) bleeding from the gastrointestinal tract, (2) venous mesenteric thrombosis of small bowel requiring resection, (3) rupture of an ulcer of the sigmoid colon and (4) pancreatitis, and (5) abdominal pain.

CASE 1.—*Bleeding from gastrointestinal tract in lupus erythematosus.*

A 77-year-old white widow was admitted on April 29, 1954, with hematemesis. Four days earlier she had developed severe weakness, which had confined her to bed. The following day she became nauseated and began to vomit. At first the vomitus was clear, but for two days it had consisted of fresh and slightly changed blood. She had paid no attention to her stools. She had no abdominal pain, anorexia, weight loss, or jaundice.

For the past five years, she had had a red scaly rash on both cheeks and over the bridge of her nose. For one year she had noted an increasing weakness and a tendency to faint. At the age of 29 she had had erysipelas. In childhood she had had severe diptheria. She had had nine children, eight of whom were living and well. Her family history was noncontributory.

Examination.—The patient was pale, obese, and in no apparent distress. The temperature was 98.6 F; pulse rate, 80, and blood pressure, 188 systolic and 68 diastolic. Over both cheeks and over the bridge of her nose was an erythematous slightly elevated, indurated rash, with the typical "butterfly" distribution. Her skin elsewhere was thin; its turgor, poor, and a number of scattered senile keratotic lesions and nevi were present. There was slight desquamation over both ears. A few moist rales were heard in her chest and a systolic murmur was heard over the apex of her heart. The abdomen was normal. The liver and spleen were not enlarged. The vomiting ceased after 20 hours, but the stools remained tarry for 12 days. She was afebrile except for a slight rise in temperature after transfusions. An upper gastrointestinal x-ray, on her fifth day, showed a small hiatal hernia and a moderate-sized diverticulum of the third part of her duodenum, which retained barium for more than six hours.

Further Course.—The patient left the hospital on the 13th day in good condition. Since then she has been in good health and has had no further hemorrhages. She is still under the care of a dermatologist for chronic discoid lupus erythematosus.

Comment.—Sixty years ago Osler collected and reported 11 cases under the title "On the Visceral Complications of Erythema Exudativum Multiforme."[18] Two further similar reports followed in later years, making a total of twenty-nine cases.[19] Most had gastrointestinal crises with colic, usually with vomiting and diarrhea. In some, hemorrhage from the bowel occurred, and in others, hematemesis. Osler also cited a fatal case of Silberman's, in which at autopsy a perforation of the stomach was found. This series of cases has been mentioned by some authors as examples of collagen disorders with visceral complications. Some of Osler's cases were probably those of collagen disease. However, today erythema exudativum multiforme (Hebra) is not considered to be a collagen disease.[22] Osler's report, nevertheless, served to stress the importance of the abdominal complications of these disorders.

The relationship of so-called discoid lupus to disseminated lupus is still a controversial question. Some would regard the former as a distinct and different entity, especially because of its better prognosis. Others have

Fig. 2.—A case of Disseminated lupus erythematosus, showing pleural and pericardial effusions and small patchy densities in the right lung base. (Reproduced with permission from Garland and Sisson,[16] *The American Journal of Surgery*, New York.)

shown that the localized discoid type may become transformed into the disseminated type as a result of various kinds of stimuli, notably exposure to sunlight and x-ray, sulfa drugs, bismuth, gold, and operations. A number of reports of acute dissemination of lupus following tooth extractions have appeared. Necessary operations, such as laparotomies, however, have generally been well tolerated. Both favorable and unfavorable effects of pregnancy have been reported.

In our Case 3, the patient was treated from the age of 15 for 22 years for a localized lesion of the fact before evidence of dissemination occurred.

CASE 2.—*Venous mesenteric thrombosis of jejunum requiring resection**

A 52-year-old white man entered St. Luke's Hospital in August, 1952, writhing in agony from intense, generalized abdominal pain which had begun suddenly a few hours earlier. In July, 1951, he had been hospitalized for epigastric pain which had been present off and on for 15 years. X-rays revealed a duodenal ulcer. He was relieved by conservative measures and dismissed but returned to the hospital the following month with fever, weakness, and generalized arthralgia, his ulcer having become quiescent. At that time, the diagnosis of disseminated lupus erythematosus was considered, in spite of the absence of a typical rash, supported by the following findings: a white blood cell count of 4500, with 11% eosinophils, negative blood cultures, an elevated sedimentation rate, a reversal of the A/G ratio, anemia, and cervical adenopathy. These, added to those of mild albuminuria and hematuria and narrowing of the retinal vessels and anemia, which were found on previous entries, in 1948 for the ulcer and in 1944 for a hemorrhoidectomy, led to the above conclusion, although at no time had L. E. cells been found in either the blood or bone marrow prior to the present entry, when an occasional L. E. cell was found in the buffy coat of the peripheral blood. Consequently, the patient had been treated with steroids for about a year for lupus prior to this acute episode and he felt well.

Examination: The patient was perspiring, but the pulse, blood pressure, and temperature were fairly normal. There was a rebound tenderness and reduced peristaltic sounds throughout the abdomen. A plain roentgenogram of the abdomen revealed no free air, but there was a distended loop of small bowel in the left upper quadrant. The white blood cell count was 17,000, with 1% eosinophils. Perforation of an ulcer was suspected, and the patient was operated upon. Serosanguinous fluid was found in the peritoneal cavity. Three feet (90 cm.) of dark, congested, edematous lower jejunum with its thickened, edematous mesentery were resected. In the immediate postoperative period, oliguria, hypotension, and a rapid pulse occurred but responded to steroids, and a good recovery followed. The patient was discharged on 6 units of corticotropin (ACTH) b. i. d. and 2 gm. of salt daily.

The noteworthy gross findings in the resected bowel were large mesenteric venous thrombi, congestion, and hemorrhages in the mesentery and discoloration of the serosa. Microscopically, mucous membrane hemorrhages with erosion of the villi, edema of submucosa, perivascular hemorrhages with necrotizing angiitis about the venules, infiltration of inflammatory cells in the vessel walls, and arterial adventitial fibrosis were all noted. The pathologic diagnosis was acute necrotizing angiitis of small bowel compatible with disseminated lupus erythematosus and venous mesenteric thrombosis (Fig. 5).

The patient was subsequently admitted with symptoms and signs of a bleeding ulcer. Hematemesis and melena were present. He had been taking 15 units of corticotropin b. i. d. He had slight hepatomegaly, anemia, and 4+ glycosuria, with a blood sugar level of 253 mg. per 100 cc. X-ray revealed duodenal ulcer and pylorospasm. He was treated conservatively for the ulcer and given insulin. He improved and was discharged

*Reported through the courtesy of Dr. E. Bruck and Dr. Otto Pflueger.

on an ulcer regimen, 20 units of insulin, and 8 units of corticotropin daily.

Comment.—In recent years, an increasingly larger number of cases of systemic lupus erythematosus, such as the preceding case, are being recognized in spite of the absence of the typical butterfly facial lesion, which is present only in about 65% of cases. The confirmation of such diagnosis by the finding of L. E. cells may require repeated examination of both the blood and bone marrow over a considerable period of time. Refinements of technique, as the introduction of the L. E. phenomenon test of Hargraves, may facilitate diagnosis.

The difficulties of therapy of lupus by steroids were further increased by the presence of a duodenal ulcer of many years' prior duration in this case.

CASE 3.—*Pancreatitis and perforation of an ulcer of sigmoid colon in lupus*

A white housewife, aged 40, entered the hospital first on June 7, 1954, complaining of intermittent attacks of moderate noncolicky epigastric pain of three years' duration. The pain radiated to her back and lower abdomen, would occur particularly in the morning, and was steady and moderately severe. She vomited frequently during these spells but had never noted blood either in her vomitus or stools. She was usually constipated, had a poor appetite, and had recently lost a few pounds. Her menstrual periods were regular but scanty. Ever since the age of 15 she had been treated, at the University of California Clinic, for a skin lesion of her face diagnosed as discoid lupus erythematosus. Her tonsils were removed at the age of 20, and her Fallopian tubes were ligated five years later. Her family history was irrelevant.

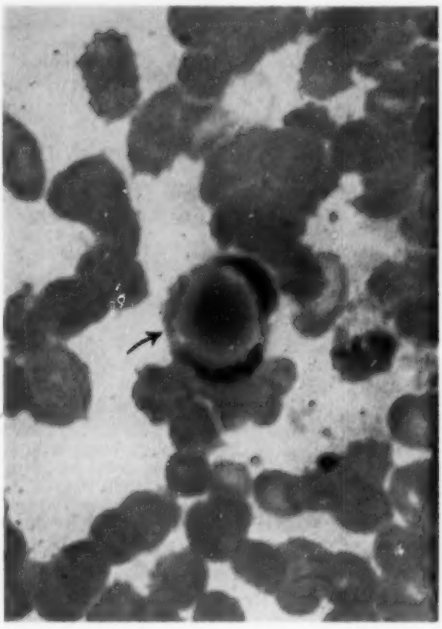
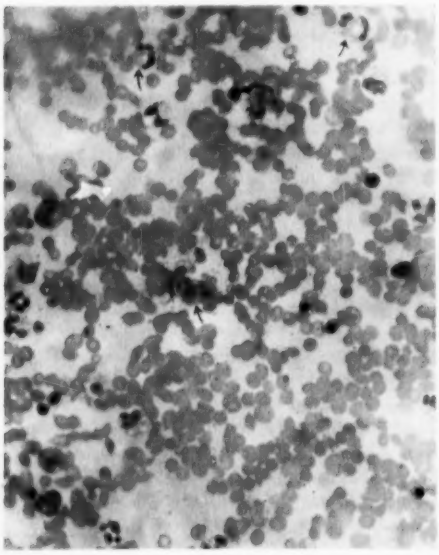


Fig. 3A.—L. E. cells, high-power magnification.

Fig. 3.—L. E. Cells (indicated by arrows), slightly larger than neutrophilic granulocytes, containing in their cytoplasm round homogeneous bluish-purple masses (Wright's stain), without evidence of chromatin structure, which appear to have displaced the crescentic-shaped, banded nuclei toward their peripheral parts. (Courtesy of Stanley Cohen.)



While she was in the hospital, her temperature rose occasionally from 99 F in the morning to 100.4 F in the afternoon, her pulse rate was 96, and her blood pressure was normal. An erythematous scaly rash was present over both cheeks, the nose, forehead, anterior cervical region, back, forearms, hands, and knees. Lymph glands were palpable in both posterior cervical triangles. The lungs were clear, and the heart was normal. There was tenderness and moderate rigidity across the upper abdomen but no palpable masses. The liver and spleen were not enlarged. Laboratory examination showed elevated serum amylase (341 units). The red blood cell count was 3,930,000, with 11.6 gm., or 69%, hemoglobin, WBC 10,000, with 69% polymorphonuclear cells. A glucose-tolerance test showed a diabetic curve. The

icteric index was 10.9. The urinalysis showed a trace of albumin, a trace of sugar, and an occasional white blood cell. No L. E. cells were found in the blood smears. The serum proteins were albumin 3.9 gm. and globulin 2.0 gm. X-rays with the dye showed a normally functioning gallbladder without stones. An upper gastrointestinal x-ray was negative. The pain gradually subsided, and the patient left the hospital considerably improved on the 11th day, with a dismissal diagnosis of recurrent pancreatitis, complicating systemic lupus erythematosus.

Six months later, she was readmitted with violent symptoms. Severe pain in the lower abdomen, radiating into the pelvis, had occurred with a sudden onset that morning. She gave herself an enema, without relief. Since her previous admission, she had had frequent attacks of generalized abdominal pain. For the past four days she had vomited occasionally. Examination revealed a desperately ill patient in shock. There was board-like rigidity and generalized tenderness but no distention of the abdomen. Peristaltic sounds were absent. The pulse rate was 120; the systolic pressure, 76, and diastolic pressure, 50. The temperature was 97 F. A flat plate revealed free air to the right of her liver. Her white blood cell count was only 3700, with 83% polymorphonuclear cells, 53% of which were stab cells, 16% lymphocytes, and 1% monocytes. RBC count was 4,500,000, with 13.7 gm., or 98%, hemoglobin, probably owing to hemoconcentration. Urinalysis was negative except for many hyaline casts. Serum amylase was 199 units. L. E. cells were again looked for in blood smears, but none were identified.

After correction of shock, the patient was taken to surgery with a diagnosis of a perforated peptic ulcer. An upper right rectus incision was made. A tremendous gush of brownish thin peritoneal fluid occurred. No lesions were found in the stomach or duodenum. The incision was then extended downward, exposing a large perforation in the midsigmoid colon. A second incision in the lower midabdomen was then made through an old laparotomy scar, and the ruptured sigmoid colon was brought out through this and the bowel sutured to the skin to exteriorize the perforation. The postoperative course was stormy. Ten days later, a subdiaphragmatic abscess was drained posteriorly. Fever, sepsis, and evidence of peritonitis continued, and the patient died on the 13th hospital day.

Microscopically, the bowel wall adjacent to the perforation showed (*a*) marked edema and focal thickening of collagen fibers in the submucosa; (*b*) marked infiltration of eosinophils, lymphocytes, and a few macrophages in both the submucosa and muscular layers, and (*c*) thick deposits of fibrin together with neutrophils, eosinophils, and lymphocytes on the serosal surface.

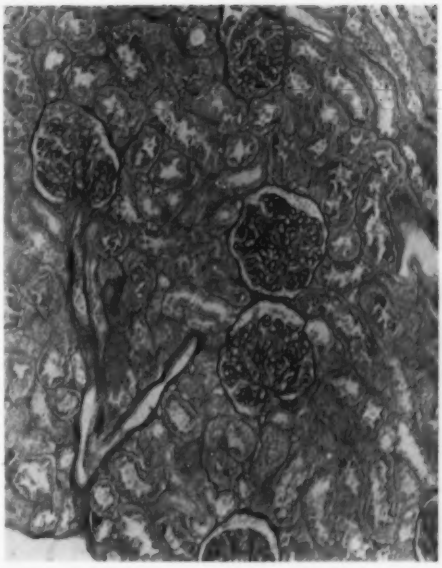


Fig. 4.—"Wire loop" lesions in renal glomeruli in disseminated lupus erythematosus. Periodic acid-Schiff stain. Note thickening of basement membrane in glomerular tufts. (Courtesy of John Frerichs.)

At autopsy the following findings substantiated the diagnosis of disseminated lupus erythematosus:

1. The rash as described above
2. "Wire loop" lesions in the renal glomeruli[4] (Fig. 4)
3. "Onion peel" lesions in the spleen, consisting of lamination of periarteriolar fibrous connective tissue[4]
4. Polyserositis: (*a*) acute and chronic fibrous pleuritis; (*b*) acute fibrinous pericarditis.

Multiple abscesses were found throughout the abdomen and in the subdiaphragmatic and pelvic areas.

Comment.—The patient had had considerable treatment with cortisone. Ulcers in the stomach occur from such treatment, and perhaps ulceration of the colon may occur, although this is unlikely, and we are not aware of any reported case.

The low white blood cell count found even in the presence of the extremely severe abdominal insult is characteristic of lupus. Hypersplenism, as mentioned later, often supervenes in lupus, and splenectomy may

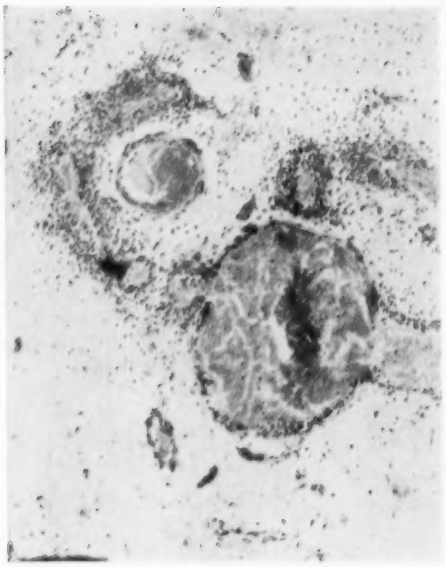


Fig. 5 (Case 2).—"Necrotizing angiitis" in mesenteric vessels in disseminated lupus erythematosus, producing gangrene of ileum. (Courtesy of Melvin Black.)

result in at least temporary improvement in such cases.

The difficulty of finding the L. E. cell is again illustrated in this case. Repeated examinations may be necessary to detect these.

Abdominal Pain in Lupus

Inflammation of serous membranes from degenerative changes in the underlying collagenous layer frequently occurs in lupus, giving rise to pleural pain and exudates when occurring in the chest and to diffuse, obscure, and puzzling abdominal pain when affecting the peritoneum.

Case 4.—A 35-year-old white housewife was admitted in May, 1955, with severe pain throughout her left abdomen, chills, and a temperature of 102 F. For 15 months such attacks had recurred practically every month just prior to the onset of her menstrual period; they would last about four days, subsiding after the onset of her period. Sometimes the attack would occur at other times of her menstrual cycle. Occasionally she was nauseated and vomited during these attacks. Between attacks her temperature was usually 99 F in the afternoon, and she felt tired and weak but was able to do her housework. Her stools tended to be slightly loose and occasionally contained a little mucus. She had one child 12 years old and a second 8 years of age. The second pregnancy had been complicated by an acute thrombophlebitis of the left leg. Examination revealed a moderately well-nourished patient with a flushed reddish tinge over both cheeks, with a temperature of 102 F, pulse rate of 96, and normal blood pressure. In both posterior cervical triangles several palpable nodes, about the size of Lima beans, were present. The lungs were clear, and the heart, normal. There was diffuse tenderness but only slight guarding over the left abdomen, particularly over its lower portion. Pelvic examination was negative except for tenderness in the cul-de-sac and left adnexal region, but no mass or induration was present. Laboratory findings: The white blood cell count was 8000, with 70% polymorphonuclear cells during the fever. Agglutination tests for brucellosis, typhoid, and paratyphoid were negative. Smears for malaria were negative. Repeated blood cultures were negative. Lupus cells were looked for in the blood and bone marrow, but none were found. Two tuberculin skin tests were negative. Proctoscopic examination, chest plates, flat plates of the abdomen, intravenous pyelograms, and examination of uterine tissue obtained by curettage were all negative.

However, a tentative diagnosis of systemic lupus erythematosus was made, based on the following facts and findings:

1. Recurring episodes of fever, in the premenstrual cycle (premenstrual exacerbations are common in lupus)
2. The low white cell count during the fever
3. A reversal of the A/G ratio; albumin 3.8 gm. per 100 cc., globulin 3.9 gm. per 100 cc.
4. Cervical adenopathy (biopsy showing only nonspecific changes)
5. Perivascular infiltration in the eye grounds
6. Occasional red blood cells and traces of albumin in the urine
7. A suggestive faint rash on both cheeks, and
8. The clinical picture as described above.

It had been suggested that this patient be explored surgically. However, we hesitated to do this because of the fear that even more marked dissemination of her disease might occur, although others have reported that laparotomies have been well tolerated.

Comment.—Because of the predominance of females affected by lupus, because of the premenstrual exacerbations, and because testosterone occasionally has had a favorable effect on this disease, a hormonal factor has been suspected. Bilateral oophorectomy in

two cases was found by Ormsby to be followed by some temporary improvement but has been abandoned.[17] Irradiation of the ovaries has been tried, but this too has been discontinued. Exposure to x-ray itself is dangerous and may cause serious exacerbation of this disease.

Periarteritis Nodosa, or Necrotizing Angiitis

Injury to the walls of vessels, with the formation of aneurysms, is an outstanding feature of this disease. Rupture of such vessels, in the following case, led to the suspicion of an acute surgical abdomen.

CASE 5.—*Retroperitoneal hemorrhage in periarteritis nodosa*

A white man, aged 49, was admitted May 30, 1945, after a fainting attack at his home. He had had no acute pain preceding this attack, but off and on for the previous three weeks he had had a dull deep ache in the left side of his abdomen which radiated slightly upward, toward his chest. The attack of syncope lasted about one hour. He had had no previous similar attacks. Three months previously he had been digitalized because of cardiac decompensation due to hypertension. In 1938 he had been treated for pulmonary tuberculosis, which became arrested. In 1939 an appendectomy was performed for acute appendicitis.

Examination: The patient was now conscious, pasty, cold, clammy, and propped up in bed, with labored respirations. The temperature was 100.4 F; pulse rate, 90, and the blood pressure, 130 systolic and 90 diastolic (usually it was 200/140.) At this time he had no abdominal pain, but there was guarding and tenseness of the entire abdomen, without tenderness. No masses were palpable. Peristaltic sounds were reduced. There was a McBurney scar in the right lower quadrant. Rectal examination was negative. Conjunctiva were pale. The funduscopic examination revealed small tortuous moth-eaten arterials with A-V nicking, slight exudates, and hemorrhage. The tonsils were enlarged. Voice and breath sounds were diminished over the left posterior chest. The heart was moderately enlarged. The EKG revealed multiple supraventricular and ventricular ectopic beats, indicating moderate myocardial damage with left ventricular hypertrophy and strain. The extremities and their reflexes were normal. The packed cell volume was 35%. The white blood cell count was 20,000, with 90% polymorphonuclear cells. The blood urea nitrogen was 74 mg. per 100 cc. The urinalysis revealed 3+ albuminuria, with many granular casts. The serologic tests were negative. The spinal fluid was normal except for a trace of protein. The chest x-rays showed an enlargement of the heart, bilateral pulmonary hyperemia, and a suggestion of infiltration of the right lower lung fields. The KUB examination showed a homogeneous grayness of the left abdomen. An acute surgical abdomen was suspected, but because of the patient's cardiorenal status it was felt that surgical exploration was contraindicated. A progressive deterioration occurred, with increasing edema and respiratory embarassment, and the patient died three weeks after entry. Autopsy revealed an organized hemorrhage in the left retroperitoneal area. Some free blood was found in the peritoneal cavity. Myocardial and renal changes were marked. The anatomical diagnosis of periarteritis nodosa was made, based on the following findings:

(*a*) Multiple aneurysms and venous thrombosis of the visceral arteries

(*b*) Characteristic microscopic findings in the small vessels

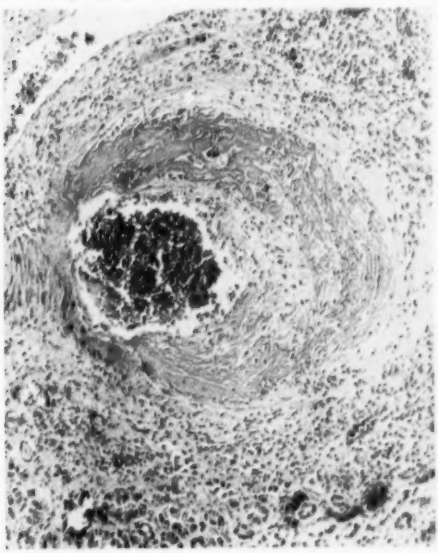
(*c*) Thrombosis of the periprostatic veins

(*d*) Recent adrenal infarcts

(*e*) Organizing retroperitoneal hemorrhage and recent introperitoneal hemorrhage

(*f*) Diffuse arteriolar atherosclerosis with secondary degenerative changes in the heart and kidneys.

Fig. 6.—Periarteritis nodosa. Slide from kidney, which shows fibrinoid degeneration of media and inflammatory infiltrate of adventitia with lymphocytes, monocytes, eosinophils, and giant cells. (Courtesy of John Frerichs.)



Comment.—Multiple system involvement of periarteritis nodosa is again illustrated in the above case. The diagnosis was not made prior to autopsy. The picture of cardiovascular-renal disease predominated, thus masking the underlying pathology of periarteritis nodosa.

A chronic duodenal ulcer was found at autopsy, as has also been noted in other cases of periarteritis nodosa, suggesting a relationship that is more than coincidental. In retrospect, the only signs that might have suggested periarteritis were the funduscopic findings, the x-ray findings of the chest (Fig. 1), which, as Garland pointed out, may sometimes be characteristic,[10] and the consideration of the pain as perhaps being due to a ruptured aneurysm, which is common in the smaller vessels in periarteritis nodosa.

Acute appendicitis or acute cholecystitis may be simulated by a form of this disease, six cases of which were reported by Donnelly and Campbell in 1954.[6] Abdominal complaints may be the first or only manifestations in some cases. They pointed out that pathological changes characteristic of periarteritis may be localized to the arteries of the appendix or small bowel, and, in some of these cases, generalized disease may never develop. It is their routine now, when a diagnosis of acute appendicitis is made and the appendix appears normal, to examine the mesentery of a large segment of the small intestine for signs of periarteritis, which usually there manifests itself by nodular masses surrounding the medium-sized vessels. In addition to the examination of the appendiceal artery, they also seek evidence of generalized involvement by biopsy of the gastrocnemius muscle (Fig. 7).

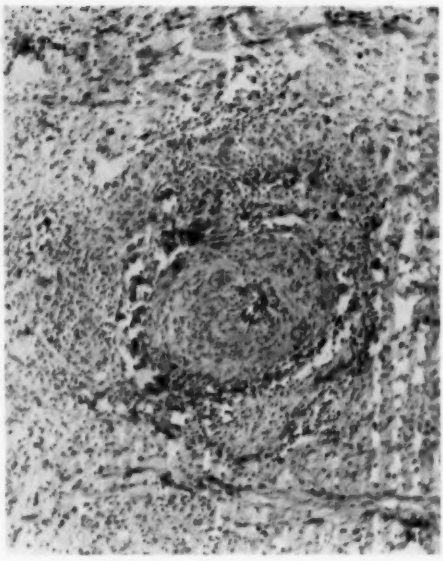


Fig. 7.—Periarteritis nodosa. Biopsy of tender skin nodule of leg. Section of small artery shows marked endothelial proliferation and severe inflammatory reaction involving vessel wall and surrounding tissue. (Courtesy of L. Zundell and R. J. Kleinhenz.)

Case 6.—*Splenectomy for periarteritis nodosa*

Prior to her splenectomy, on July 29, 1952, a 50-year-old white nurse had entered the hospital eight times over a period of 18 months and had remained for from five days to three and one-half months. Her principal complaints and signs had been multiple painful tender swollen areas and nodules on all parts of her body; chest pain; diffuse abdominal pains; edema of her legs and feet; anemia; occasional bouts of fever, sometimes accompained by chills, and occasional asthmatic attacks. Episodes of these symptoms would recur and subside. Showers of painful nodules appeared at variable intervals and would fade after a week. Some of these were slightly ecchymotic. With these the temperature usually rose to about 102 F, sometimes higher. Prior to 1951, she had been treated off and on for arthralgia of various joints. In 1945 all of her pelvic organs had been removed for a severe extensive endometriosis. Laboratory findings: On June 2, 1951, the red blood cell count, which was characteristic, was 3,740,000, with 10.8 gm. of hemoglobin, or 72%; the white blood cell count was 13,800, with 70% polymorphonuclear cells. Eosinophils usually were low or absent but appeared up to 6% at times, and once, during an asthmatic attack, rose to 12%. The sedimentation rate was 48 mm. in 60 minutes. Urinalysis was usually negative except for an occasional red blood cell. Blood transfusions were given at intervals. In May, 1951, cortisone therapy was begun, with only slight and temporary improvement. Because of the development of marked edema of the legs, it was stopped. In October, 1951, several nodules were excised from the buttocks, and in January, 1952, a nodule was taken from her leg for biopsy. These were interpreted at first as multiple foreign body granulomata with marked fibrosis. A study of further sections

revealed marked changes in and around blood vessels in the subcutaneous tissue, with marked narrowing of their lumens, thickening of their walls, and infiltration of the walls with lymphocytes, eosinophils, and neutrophils. A marked distortion of all the tissue, by an overgrowth of fibrous connective tissue, with many histiocytes and a few multinucleated giant cells of the foreign body type, was present. The final microscopic diagnosis was periarteritis nodosa. A survey of the bone marrow and the blood by a hematologist was reported as showing a normal marrow with no evidence of hypersplenism and a blood picture not characteristic of any specific disease. A chest film in April, 1952, was interpreted as showing mild bilateral hydrothorax; discoid atelectasis at the lung bases, bilaterally, and disseminated alveolar emphysema.

Progressive deterioration occurred in spite of cortisone treatment over long periods of time. Mechlorethamine (nitrogen mustard) intravenously resulted in failure. Equine corticotropin, 40 mg. intramuscularly, was tried. Clinically the patient got worse, and the spleen became palpable. When corticotropin was discontinued, improvement occurred and the splenic hypertrophy receded. This suggested to the patient's medical advisor, Dr. W. Kuzell, that splenectomy might arrest her downward course. Reports of splenectomy in other collagen diseases lent further support to this conjecture.[9] This also had been previously proposed by her surgeon, Dr. L. Custer, because of mild purpuric phenomena associated with the nodules. After all conservative measures had been exhausted, after three and one-half months of continuous hospitalization, splenectomy was advised and accepted.

Operation.—July 29, 1952. The spleen was removed through an L-shaped abdominal incision. The upper pole of the spleen was markedly enlarged, the entire spleen being three times its normal size, weighing 375 gm. Many adhesions were present but were readily freed between the spleen and adjacent diaphragm. Microscopically the findings were consistent with periarteritis nodosa. The blood vessel walls were thickened and infiltrated with inflammatory cells. Endothelial proliferation occluded the lumen of some. Areas of granuloma were present. A biopsy of the liver, which was enlarged and had a finely nodular surface, revealed similar findings.

Postoperative Course.—Convalescence from the operation was uneventful. Progressive improvement occurred. Some fresh nodules continued to appear periodically, but these were much fewer and less painful. The patient was dismissed considerably improved five weeks after operation.

On Dec. 4, 1952, she reentered again with a severe asthmatic attack with fever, cough, and chest pain. She had improved progressively since her operation; she had had fewer nodules and these were less painful. Her attack subsided quickly, and she was dismissed five days later. She then remained fairly well for 18 months, until Aug. 6, 1954, when she was again hospitalized for four days for pain in the left abdomen. Her urinary findings were negative. A few recent nodules had appeared on her right thigh and nose. Her blood cell count was considerably better than previously; red blood cells were 4,210,000, with 77% Hb.; WBC 14,400, with 76% polymorphonuclear cells, 18% lymphocytes, 6% monocytes, and no eosinophils. Four days after her discharge she was readmitted again, with an acute thrombophletitis of her right arm, which kept her in the hospital another week. Since that time she has been on prednisone, 10 mg. daily, has been able to resume her work as a graduate nurse, and has been in fairly good health except for occasional attacks when a few tender nodules appear in various parts of her body. These acute attacks have been treated with 3 mg. of colchicine U. S. P. intravenously by Dr. Kuzell and are quickly controlled by this treatment.

Comment.—Muscle biopsy is one of the most important measures in the diagnosis of periarteritis nodosa. The specimen should be obtained from an area where involvement is present and should be of adequate size, in order to include affected vessels (Fig. 7).

A chest film may show findings suggestive of this disease, as emphasized by Garland and Sisson.[10] Cardiac enlargement, pulmonary edema, nodular densities, accentuated linear markings, hilar enlargement, or pleural effusion may be found (Fig. 1).

Splenectomy for Other Collagen and Related Diseases

Of especial surgical interest are the results of the attempts to control collagen diseases by splenectomy. In 1932 Coburn and Pauli performed splenectomies on 20 rheumatic children in the quiescent phase.[5] A follow-up study of these showed that splenectomy did not prevent recurrences of rheumatic fever. On the contrary, 9 of the 20 had recurrences induced by the splenectomy within a few hours or days after operation. They mentioned one case, a Negro child with purpura associated with acute rheumatic fever, in which a splenectomy was

performed, in which death resulted, due to an immediate acute fulminating exacerbation.

An anti-inflammatory substance from the spleen, now designated as splenin A, and a second splenic substance, which was named splenin B, and which had an antagonistic effect upon the former, were developed by Ungar at Oxford.[5] Splenin A was found in the blood serum of normal persons, and splenin B, in patients with rheumatic fever. Work by investigators with these substances later led to the postulation "that adrenocorticosteroids exert at least some of their anti-inflammatory effect by way of the spleen by causing the elaboration of splenin A," as they found that splenin A exerted an anti-inflammatory effect, but cortisone or hydrocortisone did not, in splenectomized animals.[5] The rationale of splenectomy then would be based upon the removal of the harmful splenin B, elaborated by the spleen in rheumatic fever patients, or some toxic factor in victims of collagen disorders if this substance is later found to be present, as suggested by other investigators.[14] Prednisone, used in our Case 6, apparently has a very substantial anti-inflammatory effect, even in the absence of the spleen, and appears to be the drug of choice at present.[8]

Johnson, in 1953, reported 12 cases in which splenectomy was performed in an attempt to arrest deteriorating cases of lupus erythematosus.[13] In many cases of his series, this was resorted to as a final desperate measure. His first case was that of a chronic discoid type, in which severe acute purpura developed. Response was dramatic, and the patient was well after seven years except for fleeting attacks of arthralgia and occasional facial erythema. His second patient, with fever (temperature of 104 F), purpura, and anemia, also was markedly improved, but died eight weeks postoperatively of a hemorrhage from the splenic pedicle. His Case 3 and Case 4 had favorable results with remissions at first, but relapses occurred and in Case 3 the patient died three years later and in Case 4 the patient died six months after operation. The patients in Case 5 and Case 6 improved temporarily, but both died of renal failure, the first 8 months and the second 11 months postoperatively. In Cases 7, 8, and 10 the patients lived less than one week but were desperately ill when operated upon. In Case 9 the patient lived only three months. Patients 11 and 12 are still alive, but their survival and improvement are attributed in part to the use of corticotropin and cortisone. Johnson does not advocate the indiscriminate use of splenectomy for systemic lupus erythematosus, but he does point out that for some reason a remission or improvement may occur after splenectomy and that where hypersplenism, with purpura, anemia, leukopenia, and thrombocytopenia, complicates the disease, as it so frequently does, splenectomy may result in marked improvement of the blood picture and clinical condition. Except in the case of the chronic discoid type, in which the prognosis as to life is usually good anyway, the ultimate course of the disease does not appear to be altered by splenectomy.

The finding of megakaryocytes in the bone marrow has been thought essential to a satisfactory result from splenectomy in cases of hypersplenism. However, we have recently had one case in which no megakaryocytes were found by very competent hematologists, in which splenectomy was done in desperation for a severe purpura hemorrhagica. Platelets immediately increased dramatically, and the purpura was improved markedly. The patient eventually died of a reticulum-cell sarcoma of the bone marrow.

Bach and Jacobs in 1951 reported their results of splenectomy in 11 cases of rheumatoid arthritis.[2] These were divided into three groups, three done in 1938, two in 1944 and 1945, and six in 1949 and 1950. In the first case, in Group 1, improvement occurred and the disease remained inactive. The second patient was improved for six years, then died of intercurrent complications. The third case was lost to follow-up. Both patients of the second group improved

remarkably. In the last group the immediate results were disappointing, but a follow-up study 8 to 13 months later showed "that one case, previously acute, had become quiescent, four cases had improved, and one had had a slight relapse but was better than before operation." These authors "make no claim for this form of therapy, which we consider entirely experimental in nature, especially as we have no similar series of rheumatic arthritis patients who have been operated upon for other reasons for comparison." These authors also give a pertinent review of the literature, which suggests an endocrine function of the spleen.

CASE 7.—*Arterial mesenteric thrombosis in Sjögrens disease, a variant of rheumatoid arthritis*†

A 51-year-old man entered the hospital on Dec. 25, 1951, complaining of abdominal pain, vomiting, fever, and loose stools. His attack had begun two weeks earlier, had subsided after one week, but then recurred with increasing violence. In September, 1947, he had had an acute coronary occlusion for which he remained in the hospital one month. In April, 1949, he had been hospitalized for a month for an eye condition which began with acute inflammation of the conjunctiva with purulent discharge, photophobia, and blepharospasm. Later an excessive dryness of the conjunctiva developed and sicca disease (Sjögren's syndrome) was diagnosed. At that time, his blood cholesterol was 282 mg. per 100 cc.

In August, 1950, he was again admitted for severe left chest pain of sudden onset. A pleurisy with effusion was found, attributed to an infarct. A blood culture then was positive for nonhemolytic streptococci. The same organism was found in his sputum. All his teeth, which were bad, were extracted, and cultures of these also showed this organism. He improved and was dismissed but reentered after a week with upper abdominal pain, temperature up to 102 F, and pulse rate of 104. An upper gastrointestinal series revealed a large duodenal ulcer. His serum amylase was 67 units. He was dismissed after three weeks, greatly relieved by diet and medication.

Examination: Dec. 25, 1951. The patient appeared to be in great distress, with abdominal pain and vomiting. There was tenderness, moderate rigidity, some distention, and reduced peristaltic sound throughout the abdomen. The temperature was 100.4 F; pulse rate, 78, and respiration rate, 20. He improved temporarily, and the pain and distention diminished for a few days but later recurred. On Jan. 2, 1952, he was operated upon with a preoperative diagnosis of a small bowel obstruction, possibly secondary to acute appendicitis. A transverse McBurney incision in the right lower abdomen was made, and this was later extended medially to the midline. No free fluid was found, but the lower ileum was distended, nonviable, and purplish black. When its mesentery was cut, no bleeding occurred. Six feet (180 cm.) of necrotic lower ileum was resected, and an oblique end-to-end anastomosis was made. After a few precarious days, improvement was rapid, and the patient was able to leave on the 26th postoperative day.

Since the operation the patient has been under treatment for sicca disease, or Sjögrens syndrome. This is a variant of rheumatoid arthritis, with severe keratoconjunctivitis causing a very distressing dryness of the eyeballs. Degenerative arthritic changes in his neck and knees requiring manipulation by orthopedists necessitated two admissions in 1955. Otherwise his general health has been better since his operation than before.

Was the operation a form of shock therapy which benefitted the patient, and are the encouraging early results of splenectomy in other collagen diseases attributable to this phenomenon?

The above case illustrates the multiple organ involvement of this form of collagen disease, which is also characteristic of other members of this group. First the coronary vessels, next those in the lungs, and finally those of the intestine became occluded.

Comment

Zeek has proposed the term necrotizing angiitis to describe the vascular lesions which are found in periarteritis nodosa. He points out that similar vascular changes occur in desseminated lupus erythematosus. Such lesions were present in our Case 2 of lupus (Fig. 5). Gangrene of the lower ileum in our Case 7 and rupture of the sigmoid colon in Case 3 may possibly also have been due to vascular occlusion, although reports of microscopic examinations of these tissues are not available.

Zeek also has called attention to the fact that both favorable and adverse results have been obtained from the use of cortisone and corticotropin in the treatment of periarteritis

† From the services of Drs. W. Kuzell and C. C. McRae, St. Francis Hospital.

nodosa. He believes that there are different types of this disease, which react differently to these drugs, and he urges further investigation to identify them.[21] Zeek also emphasizes the fact that arteriolar necrosis, the characteristic lesion of hypertension, must be differentiated from periarteritis nodosa but observes that the two lesions may occur together, which was possibly the case in our Case 5.

In reviewing the results of splenectomy for collagen diseases, we may say that, although the results have been inconstant, something has occurred in some of these cases to strikingly alter their course. In our Case 6, of periarteritis, splenectomy was performed after other measures had failed. Progressive improvement occurred, and the patient has been rehabilitated. Whether splenectomy is a violent nonspecific form of shock therapy or whether it causes some advantageous endocrine alteration is unknown. The striking improvement in Case 7 which followed bowel resection suggests that resection here was a form of shock therapy.

In Johnson's cases, where hypersplenism was present, after splenectomy there was a marked improvement in the blood picture, indicating in these instances that the operation had a specific hormonal effect.

Summary and Conclusions

Seven cases of collagen disease with surgical problems are presented and discussed. Four of these were cases of systemic lupus erythematosus, in which bleeding from the gastrointestinal tract, abdominal pain, mesenteric thrombosis, pancreatitis, and rupture of the colon occurred. Two were cases of periarteritis nodosa. In the first of these, retroperitoneal hemorrhage produced symptoms suggesting a surgical abdomen. The second case was presented because splenectomy was advised and performed in an attempt to arrest a steadily progressive deterioration in spite of intensive therapy. This patient has been rehabilitated.

Results of splenectomy in other forms of collagen disease are reviewed. These were variable. In systemic lupus erythematosus, cases with hypersplenism and purpura were improved but the course of the disease was not otherwise essentially changed. In rheumatoid arthritis, some encouraging results are reported. In rheumatic fever the results were disappointing.

In the seventh case, a variant of rheumatoid arthritis with sicca disease, gangrene of the small bowel developed. After resection, the patient's systemic disease improved considerably.

450 Sutter St.

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An Apparatus for Extended Aortography and Femoral Arteriography

Specifications and Roentgen Technique

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The apparatus presented here has been a great help in our aortograms and arteriograms. Complete visualization of the femoral and popliteal arteries has been difficult to obtain from aortic injections, particularly when the abdominal aorta and iliac arteries are occluded. When the block of the lower aorta and iliac vessels is long or extensive, single film exposures after translumbar injection will not demonstrate femoral and popliteal arteries because the opaque medium traveling through the collateral circulation frequently arrives in the femoral vessels too dilute or too late. Previously, to visualize the femoral and popliteal arteries when the aorta is extensively blocked, it has been necessary to operate and explore the arteries and to get films after injection of radiopaque medium into the femoral arteries.

The present apparatus has made most of these operations unnecessary, since femoral and popliteal arteries can be demonstrated bilaterally after translumbar injection. Multiple films 14×36 in. or 14×17 in. are exposed at appropriate intervals.

Other methods and makeshift tunnels have not been satisfactory.

Method of Operation

The purpose is to obtain complete radiographic visualization of the arterial system in question. This instrument is so designed that clear, detailed angiography may be performed, taking in a scope of about 36 in. of body length. We use a cassette which will accommodate a film 14×36 in. in size or, more conveniently, two films 14×17 in. placed within the cassette so their opposing edges just approximate each other. The x-ray examination can be of the vessels of any extremity or the distal aorta with femoral and popliteal arteries. A single radiographic tube of ample capacity is used and centered about 63 in. above the center of the film. For each exposure one-half of the film is exposed with a grid to insure detail and contrast for the thickest parts, while the other half is simultaneously protected by a lead sheet. By means of an external manually operated handle the grid and the lead interchange by reciprocal action in approximately two seconds, and the second exposure is made at a prearranged time interval. This exposure is also enhanced by the grid, and the previously exposed part of the film is protected with the same lead sheet. The lead and grid have 3 mm. of overlap, and for all practical purposes a complete radiographic picture of about 36 in. of continuous anatomy is recorded. After clinical evaluation of the degree of the block and adequacy of the collateral circulation, the second exposure is made at an appropriate time when the bolus of dye has arrived distally. The advantage to the long cassette is that the roentgenogram encompasses all of the anatomy except for a few millimeters where the image of the grid and lead may overlap. Two 14×17 in. cassettes can be used, but it is not recommended because the film

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separation is a minimum of 1¼ in. or 32 mm. This loss of vascular visualization possibly could represent a significant area of disease.

Specifications

Throughout the explanation of the construction of the apparatus, constant reference to Figures 1 and 2 are to be made for complete understanding. This instrument is essentially a wooden box (colloquially known as "the box") 39×18¼×4 in. in size. The sides are made of oak, the base of five-layered plywood, and the top of a clear veneered hard wood that is nonopaque to x-rays. This top was made from a discarded x-ray table top. The sections of the box are united with flat-head screws, and the heads are countersunk. Lines for patient and tube centering were grooved on the top and filled with a non-lead-base white paint. Aluminum paint is satisfactory. The base of the box has rubber bumpers on each side directed longitudinally to prevent slipping or movement of the apparatus and desurfacing the x-ray table upon which the apparatus is laid. The instrument should be painted with a lacquer, not varnish, that is impervious to alcohol and antiseptics. Because the apparatus has four sturdy sides and a secure base, the top will therefore easily support the heaviest patients.

The inside is divided into two divisions. The lower region is a tunnel that is accessible from one end only and permits the introduction of the long cassette. The cassette used is manufactured by the Buck X-Ograph Co., of St. Louis, and contains a

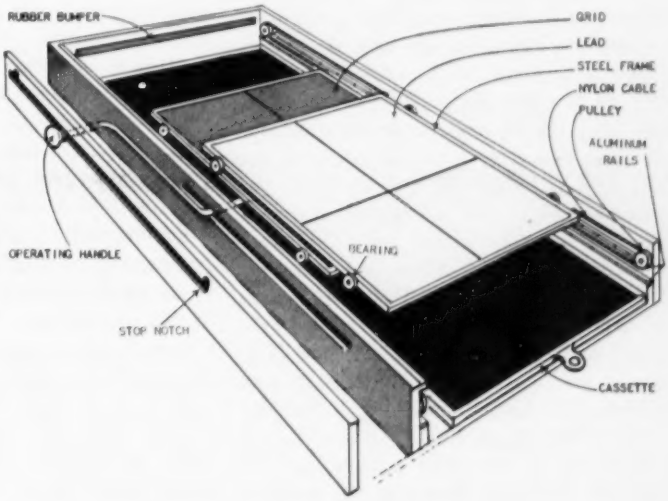

Fig. 1.—This is a three-dimensional drawing revealing the essential parts and their relationship to each other, especially the unique arrangement of the operating handle.

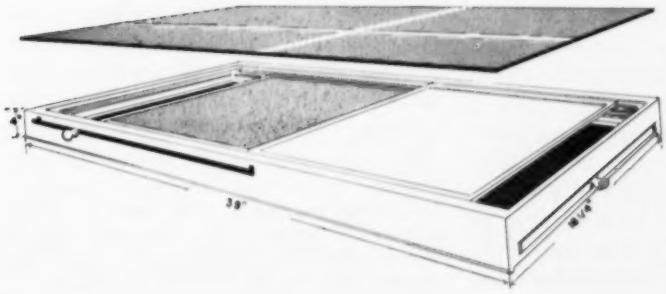

Fig. 2.—The illustration demonstrates the top removed. The crossed white lines on the top aid in x-ray tube centering. The cassette insert on the end enables easy cassette insertion, and the metal handle facilitates removal.

Radelin high-speed screen, type TF. The over-all measurements of the cassette are 37 3/16 × 15 3/16 × 3/4 in., and the size of the tunnel is slightly larger. A metal handle is welded to the end of the cassette to facilitate its removal. It is impossible, therefore, to insert the cassette incorrectly.

The upper part of the apparatus contains two movable parts: a grid and a lead sheet. The grid is manufactured by the Liebel-Flarsheim Company, of Cincinnati, and is called a Microline Grid, containing 80 laminations per inch with an 8:1 ratio. This grid is very efficient in eliminating scattered radiation. The grid we have employed has a medium focal range between 34 and 44 in., as recommended by the manufacturer. We have found from experience that the focal range can be extended to at least 63 in. and no undesirable radiographic effect can be noticed; in fact, the grid lines are hardly perceptible. Therefore we use one radiographic tube about 63 in. above the center point of the film where the grooved white lines cross on the surface of the apparatus top. The lead sheet is the same size as the grid, 15 × 18 in. and is 2 mm. thick. Because the lead is soft and pliable, it is supported on its under surface by a rigid piece of transparent plastic (Plexiglas). Both the grid and lead sheet-Plexiglas combination are firmly mounted within a steel frame about 3 mm. thick. On the sides of the metal frames are mounted small Federal Ball Bearings No. 4666. These have a diameter of 1/2 in., are 5/32 in. thick, and have a bore (center) of 3/16 in. This enables the grid and lead to travel smoothly on separate aluminum rails, 1/4 × 1/4 × 35 in. secured to the inner sides of the wooden box. The rails are 5/8 in. apart and are parallel to the cassette. To insure reciprocal action of the lead and the grid a simple pulley system is used, and the grid and the lead are connected by a nylon cable. The length of the cable is so adjusted that the nylon cord is taut at all times. This insures a positive action of interchange of the grid and the lead sheet. The pulleys are made of stainless steel and are 1/2 in. in diameter, 5/23 in. thick, and have a bore of 3/16 in. The axle for the pulley is a No. 10 screw inserted in the oak siding. The nylon cable is a 20 lb.-test limp nylon leader, type 5L, manufactured by the Wright and McGill Co., of Denver. This cable was prestretched and withstood an endurance test of 12,000 complete operations before breaking. In our experience the nylon cable proved to be the most satisfactory material to use. Steel wire, copper wire, and braided wire, respectively, either were not pliable enough, or did not withstand endurance testing, or frayed with use. The movement of the grid and lead is controlled by an operating handle which is directly connected to the metal frame of the grid. Inside both ends of the wooden box are foam rubber bumpers that absorb the shock of the moving grid and lead. This makes possible a more quiet operation and prevents excessive jarring and damage. The operating handle extends to the outside of the box. At the ends of the slot through which the operating handle protrudes are two small notches which lock the handle in place. This insures the movable grid and lead to be securely held in their proper positions at the time the radiographic exposures are made.

The weight of the apparatus is 38 lb. The construction required about 40 hours for a skilled craftsman.*

Additional equipment which is desirable includes two cushions about 18 in. square and 5 to 6 in. high. These are placed at one end, or each at separate ends of the apparatus, enabling the patient to lie on a relatively level surface. For aortograms one is placed at each end, since both the head and the feet extend beyond the margins of the apparatus. For femoral arteriograms both cushions are placed at the head end, since the entire chest and head extend beyond the margins of the apparatus. It is suggested

*L. F. Apel and J. F. Manier, machinists, Veterans Administration Hospital, St. Louis, assembled the apparatus. This apparatus will be available for purchase. For information write to Picker X-Ray, Mississippi Valley Inc., 4120 Clayton Ave., St. Louis 10, Missouri.

that the cushions be covered with a desirable surface such as "Naugahyde," medium weight, manufactured by the U. S. Rubber Co., of Mishawaka, Ind., so they are waterproof, easily cleaned, and resistant to alcohol. Since this examination is performed on top of a radiographic table, we use a cloth nonopaque immobilizer that fastens to the side of the x-ray table. This is the type which is used for abdominal compression for intravenous urography. It is adjustable and prevents involuntary motion that can result from pain due to rapid arterial dye injection. An upright portable lead screen with a lead glass window is also available to the surgeons to stand behind during the exposure (if they would only do it).

Roentgen Technique

The quality of the films in any x-ray study is of paramount importance. One main advantage to this apparatus is that two different x-ray techniques can be used: one technique for one body thickness and another technique for the remaining body thickness. Many of the "long-film" methods use one exposure, and the technical factors at times are almost impossible to adjust for a technically satisfactory study of an entire lower extremity. With our method the time and the kilovolt selectors are changed between exposures. This is a simple procedure that is expedient—especially if practiced once or twice. On control panels where the kilovolt selectors are divided into major and minor dials, a technique can be selected where the second exposure is 10 kv., or one turn of the major selector less than the first exposure. The changing of the time and kilovolt settings takes place when an assistant moves the operating handle of the apparatus. With practice and coordination a minimum of about three seconds will elapse between exposures. We have had no occasion to need a shorter interval.

The x-ray exposure factors in our department for this apparatus do not coincide with our other techniques because of the unusual distance of 63 in. (the maximal distance we can use) and the use of high speed screens (our other screens are mid speed). Therefore a technique chart for a guide for this particular study was devised. The Table represents what we have found to be satisfactory. This may not be adaptable in its entirety to other departments. However, the same type of chart can be easily assembled.

The patient is comfortably positioned on the apparatus for aortography (prone) or for femoral artiography (supine). Prelim-

Technique Chart

	Extended Aortography		
		Femoral Arteriography	
	Abdomen & Pelvis	Thigh	Leg
MA (Milliamperes)	300	300	300
Time	Thick 0.4–0.5 sec. 27–30 cm. Medium 0.3 sec. 21–27 cm. Thin 0.2 sec. 16–20 cm.	Thick 0.2 sec. 15–20 cm. Medium 0.2 sec. 13–15 cm. Thin 0.1 sec. 10–12 cm.	Thick 0.2 sec. 12–16 cm. Medium 0.1 sec. 9–11 cm. Thin 0.1 sec. 7–11 cm.
KVP (Kilovoltage peak)	Thick 85–90 Medium 77–86 Thin 75–80	Thick 75–80 Medium 72–76 Thin 69–73	Thick 69–73 Medium 62–68 Thin 60–63
Distance (in.)	63	63	63
Grid	Yes	Yes	Yes
Screen	High speed	High speed	High speed
Projection	PA	PA & AP	AP

inary films are made, and the technique and position are checked by the radiologist and the surgeon. From experience we decide, according to the clinical findings of the patient, how much delay should occur between exposures and at what phase of the injection the first exposure will be made.

The surgeon injecting the opaque medium will cry, "Shoot," near the end of the injection. The first exposure is then made. When the exposure is over, the milliammeter on the control panel will return to zero, at which time the technician will say, "Change." The surgical assistant steps up and moves the operating handle, and the grid and lead interchange. Simultaneously the radiologist will change the timer and the kilovolt selector. The surgeon, who is injecting, will cry, "Shoot," at a predetermined time interval. Then the second exposure is made. This concludes the procedure.

For short aortic blocks, the films of the thighs are exposed 4 to 6 seconds after the end of translumbar injections, whereas for patients with extensive occlusions, as evidenced by muscle atrophy and rest pain and gangrene, films of the thighs are exposed 10 to 15 seconds after the end of the injection.

For femoral arteriography no delay is needed for patients without evidence of an arterial block. A delay up to 10 seconds will be needed to visualize a clear map of the arterial tree, depending on the degree of arterial insufficiency. The amount of time elapsing from the beginning to the final inspection of the films is 25 minutes.

Summary and Conclusions

A more complete map of the arterial tree and better quality films are obtained with this apparatus. Long-film studies can be performed that encompass 34 to 36 in. of body length, the femoral artery and its branches, the distal aorta and its branches down to the knees, or the subclavian vessels and its branches.

In cases of extensive aortic block the exposure of the film of the thighs can be delayed until the media has filtered through the collateral. Two x-ray exposures are made during the examination at intervals selected for the particular patient. Each exposure will have a different technique (kilovoltage and milliampere seconds) depending on the thickness of the part. Therefore the roentgenograms are of better quality.

A grid of fine quality, having 80 laminations per inch with an 8:1 ratio, is used for better visualization and contrast.

One-half of the film is always protected with lead to prevent double exposure and/or fogging.

The apparatus protects the cassette from damage by solutions such as saline, blood, alcohol, antiseptics, or iodized media. The direct weight of the patient is on the apparatus and not on the cassette.

The apparatus is portable and can be stored in a shelf or closet when not in use.

The illustrations were drawn by W. H. French and photographed by H. L. Cradick, of the Medical Illustration Laboratory, Veterans Administration Hospital, St. Louis.

St. Anthony's Hospital, 3520 Chippewa St.

Experimental Use of Hydrocortisone in the Traumatized Knees of Rabbits

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The literature on the local use and effect of hydrocortisone acetate (Kendall's Compound F; 17-hydroxycorticosterone-21-acetate; Cortril acetate [Pfizer]) has grown to abundant proportions since Kendall et al. delivered their first laboratory investigative report in 1948 and after Hollander et al.,[1] in 1951, reported good results following the local use of compound F in the knee joint of a patient afflicted with rheumatoid arthritis.

Some confusion arose from the early reports as to the oral use of hydrocortisone. The parenteral use of the drug was thought to give satisfactory results, but Hollander demonstrated a much higher degree of prompt relief following local injection of the drug into the various involved joints.

Conn et al.[2] reported that all of the metabolic changes brought about by corticotropin (ACTH) were reproduced by the injected hydrocortisone. Other workers also drew enthusiastic conclusions as to the effectiveness of the intra-articular use of hydrocortisone for relieving the symptoms of arthritic joints, bursitis, tendonitis, and almost all noninfectious inflammatory conditions of synovia. It must be noted at this point that all conclusions had been based almost entirely on subjective clinical findings and that little or no evidence was available as to the histopathological action of hydrocortisone on affected tissues.

Ziff,[3] in 1953, after he injected joints in patients, demonstrated in the aspirated fluid, and by assay of the saline washings, that 90% of the injected crystals of hydrocortisone disappeared in one hour and were evidently absorbed and retained by the synovial membrane.

Young et al.,[4] after histological examination of a treated olecranon bursa concluded that the action of hydrocortisone was antirheumatic and anti-inflammatory. Menkin,[5] in 1954, claimed that the anti-inflammatory mechanism of hydrocortisone acted at a cellular level and impaired the activity of the injured cell so that it became less effective in producing some, if not all, of the specific chemical factors involved in inflammation. Chemical studies by DalCortivo et al.[6] indicated that clinical improvement was greatest when hydrocortisone disappeared rapidly from the synovial cavity. Ramsey and Key,[7] in 1955, developed a chemical arthritis and synovitis in the knees of rabbits and concluded, after histological examination of the tissues, that hydrocortisone not only had no harmful effect but appeared to hasten the return of injured tissues to normalcy.

Our study was undertaken after a complete review of the literature failed to bring to light any investigative work in which attempts had been made to simulate traumatic synovitis, such as athletes sustain and is often found in industry following minor re-

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From University of Virginia Hospital, Department of Orthopedic Surgery.

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Prof. Edward Corey, of the Department of Physiology, and Dr. Cornelia Hoch-Legetti, of the Department of Pathology, of the University of Virginia Medical School, gave assistance in this study.

peated trauma. We were also interested to find an explanation for the frequent complaint of pain which followed the injection, particularly in patients for whom local anesthesia had not been used.

Method

A simple apparatus was built whereby a 200 gm. weight could be dropped from a height of 1 meter onto the anterior aspects of the knees of rabbits anesthetized by intravenous pentobarbital (Nembutal). Control animals were subjected to varied amounts of force, and it was concluded that eight blows created a sufficient amount of synovial reaction to allow us to adopt a baseline for comparison. All of the animals were also subjected to a twisting of the knee joint. The femurs were locked while a strong twisting motion was exerted on the lower leg. No accurate measurements were made of the strength of the twisting force (Fig. 1).

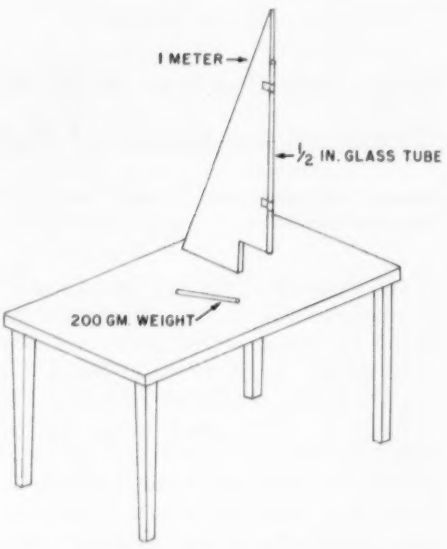

Fig. 1.—The apparatus constructed to traumatize the knee joint of the rabbit. The 200 gm. weight seen on the table was dropped a distance of 1 meter onto the anterior aspect of the knee joint.

Series I. Untreated Control Group (Seven Animals)

The knees of six rabbits were traumatized on two successive days by eight blows and eight twists. One animal was traumatized on only one day and was killed the same day. The remaining six animals were killed at 3, 5, 10, and 14 days after trauma (Table 1).

Findings in general: Synovitis manifested by hemorrhage; thickening of the synovia; inflammation, which was noted to be more chronic in the 14-day animals; fibrosis, and no real healing.

Series II. Control Group (Fifteen Animals)

The knee joints of 15 rabbits, which had had no previous trauma, were injected with 0.25 cc. of hydrocortisone. Two of the animals were injected one time and were killed at 7 and 14 days. The 7-day animal showed a thickened synovial membrane with much fibrinous exudate, while the 14-day rabbit showed very little perivascular infiltration. One rabbit was given two injections at 2-day intervals and was killed in 14 days. Histological examination revealed marked granulomatous inflammation and foreign body giant cells. Twelve rabbits were injected three times, three at daily intervals, five every other day, and four every fourth day. These were killed at 3, 5, 10, 14, and 22 days following the last injection. Histological study of the tissues led us to the

TABLE 1.—*Series I: Untreated Group*

Rabbit No.	Day of Killing	Histopathology
1	3	Hemorrhagic synovitis, synovial fluid present (gross findings, not sectioned)
16	3	Moderate subacute inflammation
18	0	Hemorrhage around muscle, slight inflammation
52	5	Marked hemorrhage with starting organization, marked fibrosis and some mucoid degeneration, a few inflammatory foci
54	10	Marked fibrosis, mild subacute inflammation
55	14	Marked chronic inflammation with hemorrhages
58	14	Slight chronic inflammation, thickening of the synovia, and marked mucoid changes

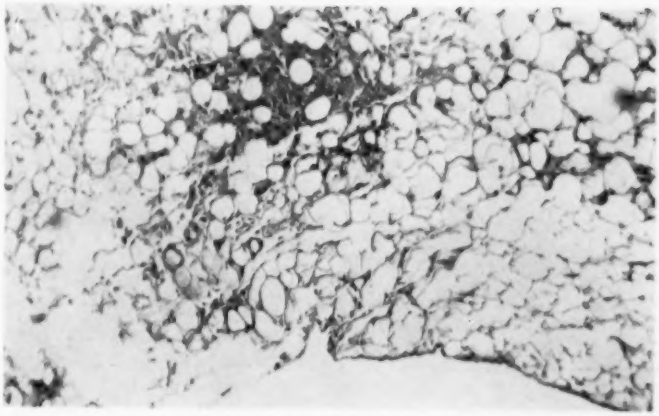

Fig. 2.—Hydrocortisone was injected twice into this knee joint at a two-day interval and the rabbit was killed 14 days after the second injection. Note the granulomatous inflammation with foreign body giant cells.

conclusion that hydrocortisone can cause a granulomatous reaction, with degenerative changes, deposition of crystals, and chronic inflammatory reaction which may persist for as long as 10 days but which may disappear before 22 days. The granulomatous reaction appeared to be more pronounced following repeated injections given at short intervals (Fig. 2, Table 2).

Series III. Traumatized and Treated Group (Ten Animals)

Ten rabbits were traumatized twice, receiving the eight blows with the weight plus eight twisting movements. The animals were injected with 0.25 cc. of hydrocortisone in from one to seven days after trauma and were killed from 0 to 10 days after the treatment. The findings in this group varied from mild inflammation with fibrosis and healing to moderate subacute inflammation and activity, indicating that healing paralled the time of killing. Definite increase in healing over the Series I control was noted (Fig. 3, Table 3).

TABLE 2.—*Series II: Hydrocortisone Without Trauma—Control Group*

Rabbit No.	No. Injections	Interval Between Injections, Days	Days Before Killing	Histopathology
71	3	2	5	Marked focal degeneration with deposits of crystals, chronic inflammatory changes in the surrounding tissues
72	3	2	5	Very marked degenerative changes with deposits of crystals, inflammation and hemorrhages, and some thickening of the synovial membrane
73	3	2	10	Chronic inflammation
74	3	2	10	Slight chronic inflammation
65	3	4	5	No pathologic change
66	3	4	5	Deposition of crystalline material with marked mononuclear reaction in the surrounding tissue, numerous macrophages present
77	3	4	10	Marked fibrosis with focal chronic inflammation
78	3	4	10	Same as rabbit No. 77
42	3	1	3	Some hemorrhage
43	3	1	14	Mild chronic inflammation, mucoid changes
44	3	1	22	No significant changes
3	1		14	Very little perivascular infiltration
4	2	2	14	Marked granulomatous inflammation with foreign body giant cells
5	3	2	14	No pathologic change
8	1		8	Thickening of the synovial membrane with much fibrinous exudate

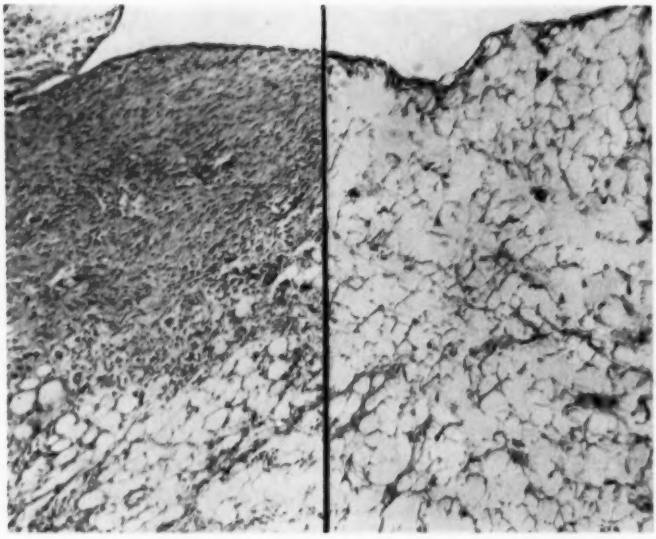

Fig. 3.—Two photomicrographs are depicted here, each of the synovia of a rabbit's knee joint which was traumatized twice; the one on the left was untreated and sectioned at 10 days after trauma, and the one on the right side is from an animal which received one injection of hydrocortisone and was killed at 9 days. Note the marked fibrosis and mild subacute inflammation on the left side and absence of reaction on the right side.

Series IV. Traumatized and Treated Group (Six Animals)

Six animals had the same type of trauma administered as was in the other groups. This group was traumatized twice on successive days, and was treated by two injections of 0.25 cc. of hydrocortisone given at two-day intervals following the trauma. The rabbits were killed at 5-, 10-, and 14-day intervals after the second injection. The animals killed on the 5th day showed subacute inflammation; the 10-day rabbits, chronic inflammation, and the 14-day rabbits, marked fibrosis with healing. In general, this group showed the best reaction (Table 4).

Series V. Traumatized and Treated Group (Six Animals)

Six rabbits were traumatized twice on successive days and were then given three injections of 0.25 cc. of hydrocortisone at two-day intervals following the last trauma. The animals were sacrificed at 5, 10, and 14 days. As compared with the preceding group, we noticed increased reaction, and we inferred that overuse of the drug was responsible for the marked granulomatous infiltration (Table 5).

TABLE 3.—*Series III: Animals Traumatized and Treated Once*

Rabbit No.	Interval Following Trauma, Days	Interval Before Killing, Days	Histopathology
2	3	0	Marked granulomatous infiltration, mononuclear type
7	1	10	Some inflammation with fibrosis, healed
59	4	4	Focal inflammatory changes, crystalline deposition, and some fibrosis of the capsule
60	4	4	Foci of subacute inflammation and slight fibrosis
17	5	7	Moderate subacute inflammation, active
19	5	7	Marked subacute inflammation, small focus of granulomatous infiltration
20	7	1	Marked fibrosis with inflammation, some collagen changes
21	7	1	Very slight inflammation
61	4	9	Less inflammation, slight fibrosis
62	4	9	Marked mucoid degeneration

TABLE 4.—*Series IV: Animals Traumatized and Treated Twice* *

Rabbit No.	Killed After Injection, Days	Histopathology
63	5	Marked focal infiltration with polymorphonuclear leukocyte infiltration and focal mucoid degeneration
64	5	Subacute inflammation in periarticular fat, focal inflammation in the tendon
75	10	Focal chronic inflammation
76	10	Fibrosis, focal chronic inflammation
10	14	Very marked fibrosis with area of necrosis, leukocytosis; healed
11	14	Moderate to marked fibrosis, few mononuclear cells; healed

* The first injection was four days after trauma. Two days elapsed between injections.

TABLE 5.—*Series V: Animals Traumatized and Treated Three Times at Two-Day Intervals and Four Days Following the Trauma*

Rabbit No.	Killed After Injection, Days	Histopathology
67	5	Ruptured tendon, macrophages over tendon
68	5	Chronic synovitis with fibrosis, foci of macrophages in the periarticular fat
69	10	Rather marked fibrosis with areas of chronic inflammation
70	10	Necrosis in tendon, some fat necrosis and chronic inflammation
12	14	Marked granulomatous infiltration, mostly in the fatty tissue, still active
13	14	Subacute inflammation, still active

Summary and Conclusions

A number of rabbits were subjected to forces which simulated in many respects the injuries sustained by athletes and by workers exposed to occupational hazards. The effects of the intra-articular use of hydrocortisone on traumatized tissues were recorded.

The local use of hydrocortisone is, we believe, a valuable adjunct in the treatment of traumatic synovitis. Its overuse may cause an irritative reaction leading to granulomatous change, and this may account for the burning pain experienced by patients after injection. The early use, followed by a minimal interval of from five to seven days before repetition, appears to offer the best results. Overuse appears to delay healing, particularly after the second injection, and may be responsible for as much inflammatory change as the original trauma. We could find no damage of the articular cartilage following the injection of the compound. If we may draw any clinical inferences, we would suggest that the use of hydrocortisone be preceeded by the injection of a local anesthetic, that at most two or three injections be given, and that a five- to seven-day intervals be allowed to pass before injection is repeated.

University of Virginia Hospital.

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Congenital Chylothorax

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Introduction

The effusion of chyle into a pleural space from a damaged or diseased thoracic duct is now a well-established entity. The development of chylothorax has been recognized for centuries [76]; yet only in the past decade have satisfactory surgical methods been devised for use in cases which have been refractory to conservative management. The various pathological circumstances which give rise to intrathoracic effusion of chyle are well documented, and so the etiology is clearly defined in most instances. However, the occurrence of chylothorax in early infancy, in the absence of other demonstrable disease and without apparent birth trauma, suggests the existence of a congenital malformation of the thoracic duct. Considered in the light of existing knowledge of the embryology and anatomy of the thoracic duct, combined with its appearance in chylothorax as seen at operation or at necropsy, there is formidable argument for accepting the idea of malformation as the underlying factor in development of spontaneous chylothorax during infancy.

Certainly, a clinical entity exists in early life with massive effusion of chyle into the chest, unattended by overt trauma or preexisting recognizable disease. Janet et al.,[36] in a brief case report in 1933, were the first to suggest that this type of chylothorax might constitute a separate syndrome. The condition has received little subsequent attention in the literature, except to be included in some series of childhood cases of chylothorax arising from multiple causes. A current review of the literature discloses 13 cases of chylothorax in infancy; to these can be added 2 additional ones from the Children's Hospital. The clinical features of this illness are intriguing; its management is complex, and the surgery of the infant's thoracic duct deserves special consideration.

Our study emphasizes the need for early surgical intervention in patients who do not readily respond to medical management. The two cases herein recorded are the first wherein congenital chylothorax has been treated by surgical means. The excellent results in both attest to the feasibility of surgical attack on the leaking thoracic duct of an infant.

Embryology

Outgrowth of the lymphatic system occurs from six lymph spaces arranged as paired jugular sacs, paired sciatic sacs, a single retroperitoneal sac, and the sac later known as the cysterna chyli. The debate among earlier embryologists as to the origins of these vascular structures was resolved by Sabin [60] in 1901. Previously, it had been held that these lymph sacs arose as discrete mesenchymal spaces from the primitive coelomic cavity. Sabin was able to demonstrate that they originated from the endothelium of adjacent veins, establishing venous endothelium as the primordial structure of the lining of the lymphatic system. Her work also corroborated that of Ranvier,[59] who had previously recognized the growth of the lymphatic system as a phenomenon of consecutive centrifugal budding. From the original sacs, buds appear as protoplasmic sprouts, following tissue planes of least resistance, progressing ever toward the periphery. The appearance would resemble many tiny beads on a string, and by subsequent fusions a network is formed with

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many tenuous connections. Beginning at the foundation sacs, division of endothelial cells produces a system which is canalized. The jugular sacs establish permanent connection with the adjacent great veins in the neck as the major lymphaticovenous communication.

The thoracic duct is probably formed from outgrowths of the jugular sacs and the cysterna chyli. However, Baetjer [5] advanced the theory of segmental anlagen occurring as multiple outgrowths of the azygos vein, which fuse to form the major portion of the thoracic duct. This has never been refuted and was further suggested by Mouchet [54] in his demonstration of multiple congenital cysts along the thoracic duct with individual fistulae into the mediastinum. That congenital anomalies of the main lymph channels occur, with resultant subsequent escape of chyle, is further emphasized by Halsted,[31] who called attention to a persisting lymphaticovenous fistula as the circumstances responsible for a huge abdominal lymph cyst. In his discussion, Dr. Halsted quotes Sabin's statement: "Thus (in this instance) the study of the development of the lymphatic system affords an explanation of anomalies involving connections between the lymphatic vessels and both the renal veins and the inferior vena cava."

During embryonic life, bilateral thoracic channels exist, each attached in the neck to the corresponding jugular sac. As development progresses, the upper third of the right duct and the lower two-thirds of the left duct become obliterated. The remaining channels persist, and by enlargement of tiny cross communicating vessels a permanent duct is formed. The multiplicity of eventual anatomical arrangements of the main duct system attests to the haphazard connections of the tiny vessels comprising the lymphatic system. It is easy to understand why congenital anomalies can occur in the couplings of such a random network.

Anatomy

That course of the thoracic duct considered "normal" by anatomists actually occurs in only about 65% of humans.[20] In this predominant form, the duct begins in the abdomen as the cysterna chyli, which is usually found overlying the second lumbar vertebral body, to the right of and behind the aorta. The duct passes into the mediastinum via the aortic hiatus, lying between the aorta and the azygos vein. The splanchnic nerve often courses immediately ventral to the duct in this area, offering confusion to the unwary. The duct passes upward in the posterior mediastinum, inclining to the left at the level of the fifth thoracic vertebra, ascending behind the aortic arch into the left side of the superior mediastinum. It then courses between the left wall of the esophagus and the pleural reflection into the neck. Arching 3 to 4 cm. above the clavicle, it swings lateralward, anterior to the subclavian, vertebral, and thyrocervical arteries, continuing into the deeper structures of the neck in front of the phrenic nerve and scalenus anticus muscle. Coursing behind the carotid sheath, the duct bends forward and empties into the junction-angle of the subclavian and internal jugular veins.

Great variations can be found in the entire ductal system. In a careful anatomical study, Davis [20] presented nine major variations of the duct. It is worthy of note that Van Pernis [69] reported a description of the thoracic duct in a series of 1081 autopsies and stated that the main duct entered the chest via the aortic hiatus between the aorta and the azygos vein in every case, although there was variation of the upper duct. This constancy has not been corroborated by other workers, and Anson [2] has illustrated 12 variations of the lower portion of the duct. A diagram of the type of duct most commonly observed (Fig. 1*A*) illustrates why leakage from the lower portion of the duct results more often in effusion into the right side of the chest whereas seepage from the upper parts of the ducts typically gives a left-sided effusion. The depiction of a double-channel thoracic duct system (Fig. 1*B*) emphasizes the difficulty which might

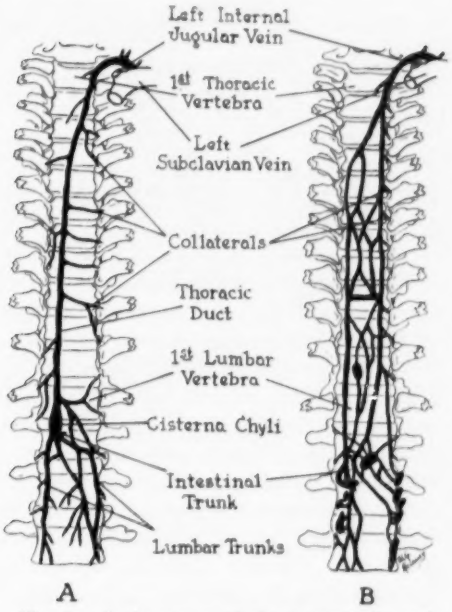

Fig. 1.—*A*, the course of the anatomically typical thoracic duct. The relationships offer a reasonable explanation for the predominance of right-sided chylothorax. *B*, one variation of a multiple channel system. The difficulty in the placement of an obstructing ligature in such cases may be readily appreciated. (Adapted from Davis,[35] *American Journal of Anatomy*, Wistar Institute, Philadelphia, 1915.)

be encountered in placement of obstructive ligatures on a leaking duct.

The collateral circulation of the lymph system and the auxiliary lymphaticovenous anastomoses have been carefully studied by Lee.[41] With ligation of the thoracic duct, anastomoses between the right lymphatic duct and the lower channels are demonstrable as well as connections between the thoracic duct and the azygos vein. Connections have been found between intercostal veins and the thoracic duct. All or any of such communications apparently may function to conduct chyle into the blood stream when the thoracic duct is ligated.

Physiology

Amphibians, reptiles, and some birds are equipped with lymph hearts for the propulsion of lymph.[34] Mammals have no such devices but are dependent on the contractility of smooth muscle in the lymph vessel walls, probably governed by the autonomic nervous system.[1] The flow of lymph proceeds at an impressive rate and may reach 200 cc. per hour.[18] That such a rate of lymph flow would be maintained continuously is unlikely, but it is certain that tremendous quantities may pour out from a severed thoracic duct or one of its branches. In addition to the muscular contraction of the vessel wall, other factors which help to maintain flow of the lymph are the following:

(*a*) the continuous influx at the lower end of the system

(*b*) valves placed at short intervals

(*c*) diaphragmatic excursion producing increased abdominal pressure, transmitted to the cysterna chyli

(*d*) concomitant increase in negative intrathoracic pressure encouraging the ingress of chyle into the thorax from the abdominal channels

(*e*) the suction effect of venous blood as it passes the lymphaticovenous anastomoses

(*f*) muscular activity of the body trunk, with milking effect on the duct

(*g*) pulsation of adjacent arteries.

The constituency of chyle explains the extreme inanition that can develop in patients with thoracic duct fistulae. It is rich in fats, conveying nearly three-fourths of ingested fat to the blood stream; chylous flow is greater after a fatty meal. Frazer[29] was able to demonstrate two routes by which ingested fat may reach the circulating blood stream, showing that the bulk of split-fat products (such as fatty acids) are picked up from the intestinal tract and carried by the portal vein to the liver, thence to the circulating blood for deposition or utilization. Unsplit fats (most ingested fat is in unsplit form) traverse the intestinal lacteals, cysterna chyli, and thoracic duct, entering the blood stream with the chyle. Thus unsplit fat apparently reaches the circulating blood through the thoracic ductal system, while predigested (split) fats enter it by an alternate route. This fact assumes real clin-

ical significance in the conservative management of a thoracic duct fistula.

As demonstrated by Co Tui and co-workers,[15] the duct is an important route over which protein is mobilized after blood loss. Working with dogs, they showed that plasma protein levels returned to normal in 48 hours after acute hemorrhage in control animals. However, the protein values did not return to normal for eight days in animals whose thoracic ducts had been previously ligated. They concluded that the thoracic duct is an important pathway by which protein from body depots is returned to the circulation.

The duct also carries a bulk of the lymphocytes to the blood stream. Since a patient with a chyle fistula has an extruded fluid which has a high lymphocyte count, the selective loss of lymphocytes usually results in a lymphocytopenia in the peripheral blood. The number of circulating eosinophils may also decrease, but this phenomenon is as yet unexplained. It may be that circulating eosinophils are decreased because of adrenocortical activity in traumatic chylothorax and that the eosinophil count will not be lower in cases of spontaneous chylothorax in infancy. No data to substantiate such suppositions are available, although it should be pointed out that in both our cases of the congenital form of chylothorax eosinophils were abundant in the peripheral blood.

Lampson [39] demonstrated a bacteriostatic quality of chyle which would seem to account for the rarity of empyema complicating chylothorax.

Chyle will separate into two distinct layers on standing, with fat seeking the upper stratum. It should be remembered that chylous fluid removed from the chest may be diluted with exudates from the irritated or injured pleural parietes, and hence values of chyle constituents may be lower than those listed in Table 1.

TABLE 1.—*Characteristics of Chyle*

1. Milky appearance
2. Separates into 2 distinct layers on standing
3. Clears when fat is extracted by alkali and ether
4. Most of the fat present is neutral (unsplit) fat
5. Odorless
6. Sterile
7. Bacteriostatic
8. Alkaline reaction
9. Fat content 0.4 to 4.0 gm. per 100 cc.
10. Specific gravity greater than 1.012
11. Protein content generally between 1.0 and 6.0 gm. per 100 cc.
12. Leukocyte count and composition vary, but lymphocytes predominate
13. Stains with any lipophilic dye which is ingested

Etiology of Chylothorax

Trauma to the thoracic duct is the principal cause of chylothorax. Chylothorax resulting from penetrating wounds or crushing injuries is easily understood; the duct or one of its branches is torn, and chyle flows into one or both pleural spaces. Many other traumatic events may befall the thoracic duct which can result in chylous effusion. The rise in intrathoracic pressure from blast injuries, and occasionally from even a paroxysm of coughing, has led to ductal rupture. In hyperextension of the spine, the thoracic duct is sometimes stretched over the vertebral bodies until it is severed. Falls, high diving accidents, and convulsive seizures are all capable of producing such hyperextension, although some authors feel that fixation of the thoracic duct to the anterior spine by preexisting inflammation must antedate such injury to produce ductal rupture. Accidental severance of the duct or one of its branches during intrathoracic surgery is becoming more frequently recognized.

In the absence of trauma, intrathoracic effusion of chyle probably occurs most frequently as a result of mediastinal malignancy. Neoplasms responsible for the formation of chylothorax may be primary or metastatic tumors which erode the thoracic duct or one of its radicles; occasionally, metastatic cells being carried in the lymph stream seem to produce an intraluminal metastasis which erodes the duct wall from within. Primary tumors of the thoracic duct are rare.

In certain instances chylothorax is attributable to infection. Erosion of the duct by a tuberculous process in the mediastinum has occurred in children as well as in adults. Other types of mediastinitis may give rise to destruction of a portion of the duct with

TABLE 2.—*Etiologic Factors in Chylothorax* *

I.	Trauma
	(*a*) Penetrating wounds
	(*b*) Crushing injuries to chest or spine
	(*c*) Spinal hyperextension (twisting falls, convulsions)
	(*d*) Precipitous rise of intrathoracic pressure (underwater blasts, coughing, etc.)
	(*e*) Surgical mishap
II.	Neoplasm
	(*a*) Primary in the mediastinum
	(*b*) Metastatic to mediastinal lymph glands
	(*c*) Metastatic foci in the intraductal lymph stream
	(*d*) Primary tumor of the thoracic duct
III.	Infection
	(*a*) Tuberculous lymphadenitis
	(*b*) Nonspecific mediastinitis
	(*c*) Ascending lymphangitis
	(*d*) Filariasis
IV.	Venous thrombosis
	(*a*) Left subclavian, left jugular
	(*b*) Superior vena cava
V.	Aortic aneurysmal erosion
VI.	Congenital anomalies of the ductal system

* Modified from MacNab and Scarlett. (47)

resultant chylous effusion, but this sequence is usually overshadowed by the effects of the existing infection. Filariasis has apparently been responsible for a few cases of chylothorax.

Isolated examples are reported wherein erosion by an aortic aneurysm or thrombosis of the great veins has been incriminated as a factor underlying chylous effusion into a pleural space.

Heretofore, the pouring of chyle into the mediastinum or a pleural space, from all causes except trauma, has been labeled "spontaneous chylothorax." It is logical to use this term for instances in adults or in older children where all extraneous factors such as trauma, neoplasm, and inflammation can be ruled out (in spite of the fact that some underlying mediastinal disease might come to light at a later time). It would seem reasonable to employ the term "congenital chylothorax" for those cases in infancy which do not have injury or other disease as an etiological agent. It is true that trauma incurred during the birth process cannot always be absolved as a cause of chylous effusion in infants. Yet in only 2 of the 15 patients in the series here studied was such a possible factor recognized during delivery of the baby. Further, if simple hyperextension of the baby during passage along a birth canal were enough to cause rupture of a normal thoracic duct, chylous effusion would probably occur more frequently than actually is the case. It is not unreasonable to postulate a congenital weakness at some point in the duct, unable to stand the strain normally imposed at delivery. A frank congenital fistula (due to failure of proper fusion of the primordial duct structures) is also an attractive hypothesis when the embryology of the duct is considered. Mouchet's [54] description of cystic dilatations of the thoracic duct which communicate with the pleural space lends credence to this theory. In this regard, the finding, in our Case B, of multiple leakage points from the duct, each of which communicated with the pleural cavity, is of particular interest.

Pathology of Congenital Chylothorax

A paucity of autopsy material makes study of the pathology of congenital chylothorax incomplete. In all four of the fatal cases in this series necropsy was performed, but in no instance was the thoracic duct visualized.

In cases of chylothorax appearing from various etiological situations, there is often a "latent period" between ductal rupture and the onset of symptoms, which has never been satisfactorily explained. The exact time between trauma to the duct and the onset of symptoms is well documented in many cases. The interval varies tremendously from case to case and has been recorded in different reports as ranging from hours to years. The most reasonable explanation for the latent period seems to be that the interval between rupture of the duct and the onset of symptoms represents the time necessary for the escaping chyle to accumulate sufficiently in the mediastinum to break through the pleura and gain access to a pleural cavity. At operations for chylothorax, either a single rent or multiple leakage points have been found in the mediastinal pleura, through which chyle is seen to emerge. That the latent

period does not represent merely the time necessary for a pleural cavity to fill up with chyle is proven by the rapid reaccumulation of chyle in the pleural sac after thoracentesis.

Four infants in this series had respiratory symptoms at or shortly after birth. This absence of a latent period might suggest the possibility of prenatal existence of chylothorax. (No autopsies performed on stillborn infants with chylothorax have been reported.) Four more of the infants developed symptoms by the end of the first week of life. In the remaining seven patients, symptoms began from 1 week to 7 months of age, after an apparently normal neonatal period.

Study of the cases in this series suggests two possible types of congenital anomaly of the thoracic duct. The first seems to be that in which there exists a series of fistulae between the duct and the pleural space, thus allowing free egress of chyle into the pleural cavity. Such an arrangement would bring on respiratory symptoms immediately after birth (without any period of latency, as in our Case B). The second type of anomaly is confined to the thoracic duct wall (with no communication to the pleurae); this may be present as a single or multiple openings in the duct, or there might simply be areas of weakness in the wall of the duct which are unable to stand the strain normally imposed on the fetus during birth. Intact mediastinal boundaries confine escaping chyle to the mediastinum initially, and thus a postnatal period of latency occurs before chyle breaks out into a pleural space, thus collapsing a lung and producing respiratory symptoms. Hence, congenital chylous effusion in infants might not manifest itself for many weeks after birth.

Clinical Picture

Symptoms.—The symptomatology of congenital chylothorax is usually so striking that the patient comes under the care of a physician early in the course of the disease. During the initial phase, symptoms of respiratory embarrassment dominate the clinical picture. Respiratory difficulty may be noted immediately after birth or may appear insidiously with a subtle intermittent tachypnea or dyspnea, which may occur only when the baby cries or is fed. Cyanosis may or may not be present. The cases having prolonged latency of symptom onset offer more diagnosis quandary. These infants may develop satisfactorily for many weeks and experience sudden collapse with a shocklike picture; dyspnea is usually then present, and cyanosis frequently attends such episodes. Nutritional depletion almost always ensues later, when the loss of chyle by repeated thoracenteses is significant.

Physical Findings.—Examination discloses a striking absence of fever in a patient with severe distress. Respirations may be suprasternal, intercostal, and subcostal areas 100 per minute and severe retraction in the is frequently seen. The involved side presents typical findings of intrapleural fluid with respiratory lag, flatness on percussion, and diminished or absent breath sounds. Shift of the mediastinum with displacement of cardiac dullness is invariably present in infants with extensive accumulation of intrapleural fluid. (Tracheal deviation is not a reliable sign in infancy.)

Laboratory Data.—Anemia is usually not a feature of the illness. Lymphocytopenia can be reasonably expected as a consequence of chyle loss, although it is not always present. The total leukocyte count is usually normal. The diagnosis should be suspected at the initial thoracentesis; it is substantiated by assay of the fluid as outlined in Table 1. Newborn breast-fed babies with chylothorax may exhibit a bright yellow stain in the chyle, which is attributed by some to the pigment, lactochrome, originating from the colostrum.[62,67]

Roentgenologic Examination.—Roentgenograms generally show massive effusion into the chest with marked compression of a lung. The relative radiolucency of fat, as previously pointed out with chylous ascites [74] might possibly suggest chyle as the type of fluid present.

TABLE 3.—*Summary of Cases*

Case	Author	Sex	Site	Age at Onset	Treatment	Age Therapy Was Begun	Frequency of Taps	Total Fluid Withdrawn, Cc.	Period of Therapy, Days	Result	Autopsy
1	Everhart	M	Right	Birth	Thoracenteses	18 days	Daily	1200	18	Died	Duct not found, single pleural leak
2	Stirlacci	F	Right	1 hr.	Thoracenteses	4 days	q. 3 d.	?	8	Cured	
3	Sakula	M	Right	2 days	Thoracenteses	5 days	q. 4 d.	135	5	Cured	
4	Martines	M	Left	4 days	?	?	?	?	21	Cured	
5	Hilgenberg	M	Left	4 days	None	--	None	--	1	Died	Duct not found
6	Stewart	M	Right	4 days	Thoracenteses*	4 days	q. 2 d.	1155	16	Died	Duct not found, single pleural leak
7	Wessel	M	Right	13 days	Thoracenteses	14 days	Daily	1278	13	Cured	
8	Forbes	F	Bilat.	3 wk.†	Thoracenteses & reinfusion	7 wk.	q. 1-5 d.	5300	60	Died	Duct not found
9	Janet	M	Right	3 wk.	Thoracenteses	4 wk.	Once	250	1	Cured	
10	Blood	F	Left	3½ wk.	Thoracenteses	4 wk.	q. 3-8 d.	590	18	Cured	
11	Watson	F	Right	7 wk.	Thoracenteses	8 wk.	Daily	2245	13	Cured	
12	Lottheisen	M	Right	8 wk.	Thoracenteses§	8 wk.	?	?	17	Cured	
13	Laplane	M	Right	7 mo.	Thoracenteses	7½ mo.	q. 3 d.	?	4	Cured	
14	Our Case A	M	Left	1 hr.	Thoracenteses & operation	10 wk.	q. 3 d.	945	24	Cured	
15	Our Case B	F	Left	Birth	Thoracenteses & operation	3 wk.	(a) q. 3 d. (b) Daily	480 560	8 4	Subsided Cured	

* Partial withdrawal of fluid to preserve intrapleural pressure relationship.
† Exact date of onset not given, but before three weeks.
‡ Left chest, 3600 cc.; right chest, 1700 cc.
§ Inferred from Janet's writing.

Summary of Cases from the Literature

A compilation of data from published cases of congenital chylothorax reveals some interesting facts, as summarized in Table 3. The selection of these cases deserves some comment because of the omission of several widely quoted examples of infantile chylothorax. Every effort was made to eliminate all overt cause which could be historically symptoms. Pisek's [58] case in a 9-week-old infant was not included because of convulsion which antedated the onset of the connected with the onset of respiratory chylous effusion. The patients of Muttermilch [55] and Gironcoli [30] had tuberculosis. The cases of Jennings,[37] Foley,[27] and Brescia [11] are each excluded because of preexisting pneumonia and severe episodes of coughing. Brescia, however, is responsible for emphasizing the occurrence of chylothorax in childhood with his collection in 1941 of 21 cases from all causes. Blood's [9] first patient seems primarily an example of chylous ascites, although this case further suggests anomalies of the main lymph channels as a cause of chylous effusion. His second case, in a 2-year-old girl, was discarded because of the inability to exclude occult trauma; whether a latent phase in congenital chylothorax may last two years (or, indeed, as long as seven months in the 13th case in the present series) is a matter of conjecture.

The 15 cases herein summarized include all reported instances of congenital chylothorax which we have been able to find. In 2 cases (Cases 1 and 14) there is a history of some difficulty during delivery; the other 13 births were apparently normal.

Ten of the fifteen patients were males, a predominance of 2:1. Right-sided effusion occurred nine times and left-sided collection six times, a ratio compatible with other series, and understandable in view of the anatomy of the thoracic duct. Bilateral chylothorax from any cause is extremely rare and occurred in only one instance in the present group of the congenital form.

Four of the thirteen cases treated medically ended in death, a mortality rate of 31%. Death occurred on the 1st, 16th, 18th, and 60th days of illness, respectively. All recoveries on conservative management were achieved by the 21st day of treatment. This suggests an appropriate limitation for any medical regimen.

There were two instances [70,71] in this series where diarrhea occurred just prior to spontaneous closure of the leak. In a third case [68] chylothorax ceased concomitantly with a diarrhea. This fact suggests that emptying the gastrointestinal tract by withholding feedings and employing gastric suction, during a conservative trial, may abet the cessation of a chyle leak, but such a therapeutic measure is as yet unproved.

Because of failure of conservative management two patients from our hospital were treated surgically; these are the only cases of congenital chylothorax which have been handled by surgical means. In Case A, no frank leak into the pleural sac was demonstrated, but the inflammation following operation apparently was sufficient to obliterate a tiny leak, because a prompt recovery ensued. Exploration of Case B revealed multiple leakage points from the mediastinum, interpreted as congenital fistulae. The definitive surgical treatment of these leaks was very satisfying and was followed by a rapid recovery of the baby.

Treatment

Nonoperative Management.—Evolution of a satisfactory treatment for chylothorax has been a slow process. Medical measures are aimed at maintenance of nutrition and ventilation in the hope that spontaneous cessation of the effusion will occur. Certainly, as Table 3 demonstrates, rescue of these children by careful conservative measures is possible in a good percentage of cases. Oeken,[56] in 1908, recognizing the extreme depletion of fat and protein in this disease, performed the first intravenous reinfusion of chyle. While it is true that Little et al.[43] were able to keep a young woman with a

chylous fistula alive for 18 months with frequent intravenous feedings of the patient's chyle, there are several reports in the literature of anaphylactic death from such a procedure. Since long-term conservative management is no longer necessary, now that surgical attack is available, the hazards attending reintroduction of aspirated chyle make this practice unwarranted. A more important contribution in the maintenance of nutrition is Frazer's demonstration of the absorption of split fats via the portal vein. Thus, with the feeding of fatty acids, the patient receives more nourishment than would be the case if only unsplit fats were fed.

Review of the 15 cases shows that conservative trial is definitely warranted. The regimen should include thoracentesis as often as necessary, the repetition of aspiration being governed primarily by the degree of dyspnea. Stewart and Linner [67] advocated the principle of withdrawal of only that quantity of fluid necessary to relieve dyspnea. They felt that the remaining fluid served as a tamponade to the leaking mediastinum but that complete drainage encouraged the flow; this has never been proved, and we have preferred to withdraw all the available fluid, allowing full reexpansion of the lung. When fluid reaccumulates rapidly day after day, an indwelling chest tube is recommended. Constant suction on the tube is unwise, because the increase in negative intrapleural pressure may tend to keep the duct fistula open. The tube is intended as an avenue which may be used as frequently as necessary to drain off the accumulating chyle by gentle aspiration with a syringe, aspiration being performed as often as might seem to be indicated.

Adequate drainage of the chest must be coupled with vigorous combat of inanition. A diet rich in protein and total calories is essential; the addition of split-fat products is a useful adjunct. Parenteral plasma is often helpful in overcoming hypoproteinemia. The use of whole blood is usually unnecessary. Dehydration is a problem when large quantities of chylous fluid are lost and must be treated with proper fluid replacement. Water-miscibile varieties of the fat-soluble vitamins are advisable. Antibiotics are added empirically, but secondary infection is usually of no consequence, because of the bacteriostasis afforded by chyle.

This course may be followed as long as three weeks if the infant (1) remains in good nutritional status, (2) maintains adequate ventilation, (3) has no evidence of infection, and (4) shows definite progress in closure of the fistula. If there is no apparent decrease in the flow of chyle toward the end of the 21-day trial, or if at any time the patient shows signs of losing ground clinically, the conservative regimen should be abandoned forthwith and the infant readied for surgery.

Surgical Treatment.—Early ligations of the thoracic duct were performed in the surgical laboratories of Astley Cooper,[14] Magendie,[48] and Dupuytren,[24] among others. One of the earliest successful reconstructions of the duct in a human was accomplished in 1898 by Cushing,[19] who repaired a chylous fistula in the neck. His report carried this conclusion: "The main part of the duct lies in a surgically forbidden region of the body." De Forest,[22] in 1907, advocated ligation of the main duct if it was accidentally severed, illustrating an early belief that patency of the main duct was not essential. In 1922, Lee [41] demonstrated conclusively that collateral lymphaticovenous channels exist in animals and described a method of intrathoracic ligation of the duct. This work apparently formed the basis for Lilienthal's [42] remarks on chylothorax in 1927: "Wide thoracotomy may be indicated with a search for the wound in the duct which may then be ligated or otherwise dealt with. The chances are good that the rich anastomoses will furnish a new channel into the venous circulation." In spite of this background, Florer and Ochsner [26] expressed the consensus of existing surgical opinion when they observed in 1945 that primary surgical attack on the leaking intra-

thoracic portion of a duct had been uniformly fatal. It remained for Lampson,[39] in 1946, to accomplish the first successful intrathoracic ligation of a human thoracic duct. This method of direct attack has subsequently been used in treatment of many cases of chylothorax. Attempted reconstruction of the duct as suggested by Hodge,[33] Seaman,[64] and others is difficult and seems unwarranted.

Thoracotomy should be performed on the side of the effusion. There are several disadvantages of always entering the right chest for supradiaphragmatic duct ligation (as advanced by Baldridge[7] and others): (1) the duct may not be visible even after careful search, precluding an effective ligation of the main trunk; (2) the anatomical variations of the duct (Fig. 1*B*) may allow continued leakage even if the main channel is ligated low in the chest; (3) of foremost importance is the fact that multiple leakage points may exist which require individual attention. Therefore, we firmly believe that it is much better to enter the chest on that side where the leak has occurred.

When multiple pleural leaks are encountered, and one is dealing with an edematous, friable mediastinal wall and chyle-soaked mediastinal structures, suture of the mediastinal leakage points may prove the wisest course. Such sutures may serve the dual function of ligation of small leaking channels as well as strengthening the pleural barrier. Both Shumacker and Moore[66] and Baffes and Potts[6] have reported success with this maneuver in cases of postoperative chylothorax in infants. In instances of chylothorax where this technique has been used, we have also elected to swab the mediastinal pleura with tincture of iodine in the hope that the additional irritating effect would aid in sealing off any tiny, unseen leaks.

Our aim in treating these cases (and patients with chylothorax from any cause) has been (*a*) ligation of the vessel at the leak whenever possible, (*b*) double ligation of the main trunk or trunks below and above the leak when the exact point of leakage cannot be ascertained, and (*c*) multiple sutures of a leaking mediastinal pleura when the fragility of the inflamed structures precludes detailed dissection of the thoracic duct system.

Procedure.—Right thoracotomy is best performed through the fifth or sixth intercostal space. This affords ready access to the lower chest and is adequate for the examination of the entire mediastinum. Isolated leaks in the mediastinal pleura should be closed by suture before the mediastinum is entered. If further investigation reveals readily identifiable mediastinal structures, these can be dissected so that the duct itself can be isolated and handled appropriately. If the mediastinal tissues are so edematous that identification of structures is difficult, the prior sutures of the pleural leaks will probably suffice to bring about a cure. If a leak through a pleural fistula or from the duct itself cannot be demonstrated, low ligation of the duct can be carried out but should be followed by prolonged inspection of the mediastinum to observe any continued leak. For better visualization of the ductal system, or finding a leak therefrom, we have, at the operating table, used subcutaneous thigh injections of Evan's blue dye (1% suspension, using 0.5 mg/kg. body weight), as suggested by Merrill.[53] Another method[38] is the ingestion of violet or green lipophilic dye, added to a pat of butter, which is eaten two hours before surgery. Visualization of a duct by injection of radiopaque medium into it for roentgenograms at the operating table[78] seems superfluous and unsatisfactory.

Thoracotomy for left chylothorax is performed through the fourth or fifth interspace, since effusion into the left chest usually originates from a more cephalad portion of the duct. All mediastinal leaks are sutured; then the mediastinal pleura is opened. If the duct is not apparent, ligation and division of regional intercostal vessels allows anterior retraction of the aorta, thus facilitating the search for the main duct in

the posterior mediastinum. Individual leaks from the exposed channels are then dealt with by appropriate closure with nonabsorbable surgical (silk) sutures.

Operative wounds in the mediastinal pleura should always be closed. The application of tincture of iodine to the areas of seepage from the mediastinal pleura is a useful adjunct. A chest catheter should remain in place for several days, to allow frequent aspiration and irrigation of the pleural space.

Presentation of Cases

CASE A.—*History.* The patient was a 9 lb. 7 oz. full-term boy; delivery was face-up breech. Heart murmur was noted soon after delivery, and, within an hour after birth, cyanosis and dyspnea were observed. The child was placed in oxygen. The fontanelle was noted to be full, and lumbar puncture revealed bloody fluid; subsequent lumbar puncture showed clearing in two weeks. The patient was unable to exist without oxygen until the seventh week. Respiratory distress continued, and the patient was referred to the Children's Hospital at the age of 10 weeks.

Physical Examination.—Temperature, 98.6 F; pulse rate, 168; respiration rate, 84. No cyanosis. Respiratory distress with marked retraction. Left chest dull. Breath sounds diminished on the left. Cardiac dullness shifted to the right. Heart enlarged with harsh systolic murmur. Liver and spleen enlarged.

Laboratory Data.—Urinalysis: Within normal limits.

Hemogram: Hemoglobin, 14 gm.; WBC, 11,800 cells per cu. mm.; differential count, 56% polymorphonuclear cells, 25% lymphocytes, 3% monocytes, 15 eosinophils; RBC normal; serum protein, 5 gm. per 100 cc.

Chest Film: Left pleural effusion with partial collapse of the lung and mediastinal shift (Fig. 2*A*.)

Lumbar Puncture: Clear fluid. No cells.

Thoracentesis: Milky fluid, containing many fat particles, protein 3.18 gm. per 100 cc.

Fat Uptake Study*: Ingested olive oil (unsplit fat), high level in chylous fluid; ingested oleic acid (split fat), small amount in chyle but good level in blood (interpreted as demonstration of the alternate route of split fat entering general circulation as described above under Physiology, q. v.).

Course.—Between the 1st and 24th hospital days, 10 thoracenteses were performed, yielding a total of 945 cc. of chyle. With no decrease in the flow, and with progressive weakening of the patient, thoracotomy was performed.

Operation (Dec. 12, 1949).—Left thoracotomy via the seventh intercostal space. There was 40 cc. of milky fluid in the pleural space. No fluid leak from the mediastinal pleura was seen, even after careful scrutiny for one hour following two injections of Evan's blue dye into the subcutaneous tissue of the leg. The mediastinal pleura was swabbed and roughened with gauze, to stir up a reaction in it and close off any small leaks which were not visible. The chest was closed without drainage. The patient recovered without reaccumulation of chyle, and no further thoracenteses were necessary.

Follow-Up.—Followed in clinic to present age of 6 years. Growth and development normal. Good general health. In first grade doing well. Heart murmur no longer present. Chest clear by auscultation and on x-ray.

* Performed by Dr. Allan Crocker after the manner of Fraser.[9]

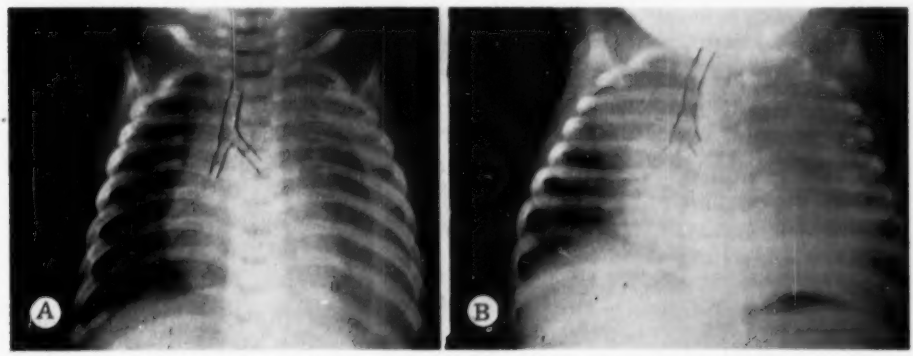

Fig. 2.—*A*, Case A, showing pleural effusion with partial collapse of the left lung, and marked mediastinal deviation. *B*, Case B, depicting massive chylothorax with displacement of the mediastinum to the right.

Comment.—There is much to suggest obstetrical trauma in this case. The absence of a demonstrable point of leakage in the mediastinal pleura is an unusual finding and is difficult to explain. There must have been a diminished chyle flow during operation which made it impossible to demonstrate the points of leakage. Postoperative pneumothorax and inflammation apparently combined to allow sealing of whatever leaks existed.

CASE B.—*History.*—A 7 lb. 8 oz. girl, the product of full-term uncomplicated gestation and spontaneous delivery without known trauma. Tachypnea, noted at birth, persisted with intermittent bouts of cyanosis. At 2½ weeks of age, the left chest was found to be dull. Thoracentesis yielded 180 cc. thick gray-yellow fluid, and the baby was referred to this hospital.

Physical Examination.—Temperature, 98.8 F; pulse rate, 150; respiration rate, 60. Cyanotic, tachypneic, with intercostal and suprasternal retraction. Breath sounds absent on the left except at apex, dullness over the lower left chest, hyperresonance over trachea, and heart shifted to the right.

Laboratory Data.—Urinalysis: Negative.

Hemogram: Hemoglobin, 13.2 gm.; WBC, 7550 cells per cu. mm.; Differential count, 60% neutrophils, 30% lymphocytes, 3% monocytes, 6% eosinophils, 1 basophil.

Chest X-Ray: Massive intrapleural effusion on left, with mediastinal structures displaced to the right (Fig. 2*B*).

Thoracentesis: Milky fluid; sterile; specific gravity 1.012; total fat 1.5 gm. per 100 cc.; 15-20 lymphocytes/HPF; 5-6 stained fat particles/HPF.

Course.—Thoracenteses were performed as follows: first day, 70 cc.; third day, 120 cc.; seventh day, 110 cc. By 14th day, formation of fluid seeming to have decreased, the patient was discharged to her physician to be closely followed for recurrence of fluid in the chest. She did fairly well for five weeks; then dyspnea gradually recurred, and she was readmitted six weeks later.

Physical Examination.—Essentially unchanged, except for recurrence of effusion on the left.

Laboratory Data.—Hemoglobin, 11.7 gm.; WBC, 7550 cells per cu. mm.; differential count, 60% polymorphonuclear cells, 30% lymphocytes.

Course.—Thoracentesis was performed three times in four days, with a total removal of 560 cc. of fluid. Because of the protracted course with no evidence of decrease of flow, thoracotomy was decided upon.

Operation (Oct. 24, 1951).—The left pleural sac was entered through the fifth intercostal space. One hundred cubic centimeters of milky fluid were evacuated. Thickening of the mediastinal pleura was noted. Several small chylous leaks from the smaller mediastinal pleura were seen. Each was sutured with silk, and each area was swabbed with tincture of iodine. The pleura was then opened low in the chest, and the thoracic duct was identified behind the descending aorta; the duct was doubly ligated with silk. The incision in the mediastinal pleura was sutured, and the chest was closed. A rubber catheter was placed in the pleural space postoperatively and attached to gentle suction. Drainage was minimal; the tube was removed on the sixth postoperative day, and the patient was discharged on the ninth postoperative day, without evidence of fluid in the chest.

Follow-Up.—Seen until 3 years of age. Chest completely clear. Growth and development normal.

Comment.—The sutures in the mediastinal pleura probably gave the control of leakage which was desired, but the low duct ligation probably was of some value in diminishing chylous flow and facilitating healing of the leaks which were sutured above this level. (It is thought that the finding of multiple leakage sites in the main duct which communicated directly with the pleura lends strength to the theory of anomalous ducts as the prime factor in spontaneous chylous effusion).

Conclusions

A definite clinical entity of congenital chylothorax exists in infancy, characterized as follows:

(1) There is effusion of chyle into a pleural space; usually unilateral but possibly bilateral in nature.

(2) The condition occurs in infants in the absence of other disease or trauma, probably on the basis of congenital anomaly in formation of the thoracic duct.

(3) Symptoms may occur at birth, suggesting prenatal effusion, or there may be a latent interval as long as several months before symptoms appear.

(4) As in other forms of chylothorax, the initial symptoms are those of respiratory embarrassment, with increasing inanition as the loss of chyle continues.

(5) The condition may be fatal but often ceases spontaneously after one or many thoracenteses.

(6) The condition is amenable to surgery if conservative measures fail.

Sixty-nine per cent of patients treated by conservative measures in this series recovered; this is considerably higher than the fifty per cent survival usually cited for other types of chylothorax treated medically. The advances of thoracic surgery for infants during the past decade are such that treatment is now available for babies with chylothorax who do not satisfactorily respond during a careful trial with medical measures. Our two patients subjected to surgical therapy have made excellent recoveries. It is hoped that surgical measures, if not delayed by prolonged clinical conservatism, will produce an increasing number of cures in the cases which are recalcitrant to a medical regimen.

Summary

A clinical study of congenital chylothorax in infancy is presented with 13 illustrative cases from the literature, to which 2 new cases are added.

Embryologic and anatomic evidence is offered for the existence of congenital anomalies of the thoracic ductal system as a factor underlying this condition.

The diagnosis and treatment of the condition is discussed, with emphasis on early surgical intervention when medical measures appear to be insufficient in bringing about a cure.

300 Longwood Ave. (15) (Dr. Gross).

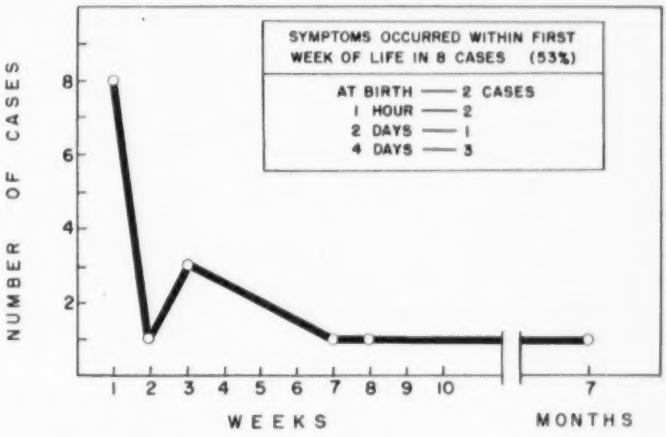

Fig. 3.—Age at onset of symptoms in 15 cases of congenital chylothorax.

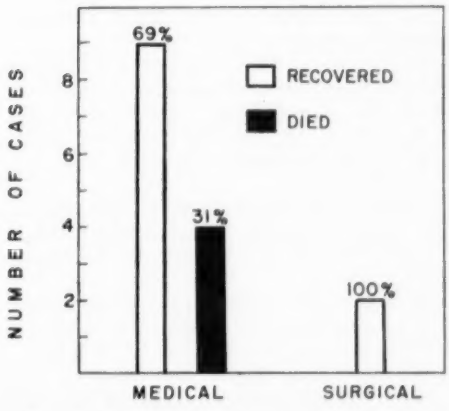

Fig. 4.—Results of treatment.

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Mucosal Carcinomas as a Result of Irradiation

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This report concerns nine patients with carcinoma arising in mucous membranes included in a field of radiation therapy; the therapy had been administered previously for benign or malignant disease of other tissues or organs. The tumors recorded here comprise six squamous-cell carcinomas—two of the hypopharynx, two of the tongue, one of the buccal mucosa, and one of the anal canal—and three adenocarcinomas—two of the colon and one of the esophagus. Six of these tumors can, with reasonable certainty, be considered a late result of irradiation; with the three others the origin in irradiated areas makes it highly probable that radiation was a basic factor in the tumor development.

CASE 1.—A 53-year-old woman was first seen in May of 1948. She gave a history of having had a malignant tumor of the left parotid gland surgically removed in 1939. This was followed by a series of external x-irradiation treatments which produced a typical telangiectasia of the skin of the left side of her face and neck. In October, 1947, a plastic reconstruction was undertaken in order to alleviate some of the deformity of the total facial-nerve paralysis. When she was first seen by us she had a squamous-cell carcinoma involving the left lateral margin of the tongue, extending posteriorly to involve the base as well as the anterior wall of the pharynx. Atrophic irradiation change in the buccal mucosa, floor of mouth, and tongue on the left was as apparent as the radiodermatitis of the skin externally.

The tumor was treated with the introduction of interstitial radon seeds, which, over the course of the next three months, produced extensive radionecrosis. The patient subsequently developed recurrent tumor locally. Terminally, massive metastases developed in the neck.

CASE 2.—The patient was a 63-year-old woman in 1947 when she presented herself for examination because of a tumor of the anal canal. In 1936 the patient had had a squamous-cell carcinoma of the cervix treated with the application of radium element, followed by a series of external irradiation treatments to the midline over the abdomen and sacral area. Biopsy of the anal canal revealed squamous-cell carcinoma. The perineal and perianal skin, and the anal canal, showed advanced radiodermatitis. Local excision of the anal tumor was done, but the tumor recurred approximately one year later. At that time a colostomy and posterior resection of the anal tumor was performed. Postoperatively the patient developed hematuria, followed by a vesical fistula; she died in anuria on the 10th postoperative day.

CASE 3.—The patient was a 54-year-old school teacher who was admitted to the hospital in May, 1948. Nineteen years previously she had become aware of a swelling in the left upper jaw, which, after biopsy, received multiple treatments, consisting of local application of radium and external x-irradiation. The initial interpretation of the microscopic material was that the lesion was an adamantinoma. At the time the patient was first seen by us she had a chronically draining, ulcerated area on the left side of the face and in the hard palate. There was no vision in the left eye, where she had developed radiation opacity of the cornea. Her pain at this time was so severe as to be almost incapacitating, although with opiates she had managed to continue to carry out her occupation to a limited degree. The radionecrotic maxilla was removed, and underneath it an extensive ossifying fibroma was found.

During the course of the next two years, two major surgical efforts at block excision were undertaken to eliminate this "benign" disease. The second of these included an enucleation of the functionless orbital contents. In spite of this the tumor remained uncontrolled.

In October, 1950, a biopsy of a nodule in the buccal mucosa revealed a new problem; squamous-cell carcinoma had developed in the tissues damaged by previous irradiation. Treat-

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ment of this new development, of course, was an obligate surgical one, since additional irradiation of these already damaged tissues was impossible. During the next two years, multicentric independent foci of disease were discovered and treated by excision. At no time was the patient without new foci of disease within a two-month interval. The irradiation-modified tissues gave way with neoplastic change practically simultaneously in areas of the gingiva, palate, and buccal mucosa. Severe pain again became the major problem as far as the patient's functional ability was concerned, and this was controlled by cervical sympathetic nerve blocks. Following one of these procedures in February, 1953, the patient developed a hemiplegia and died 14 hours later.

CASE 4.—This 48-year-old housewife was referred by her otolaryngologist because of a tumor mass involving the posterolateral wall of the hypopharynx. When she was first seen in September, 1953, she complained of a sore throat and some difficulty in swallowing during the prior six weeks. During the period from 1930 to 1943 the patient had been bothered by numerous dermatological problems, involving the skin of the upper chest and neck particularly. These difficulties had been treated by the local application of various medications but also by a number of dermatologists with multiple x-ray exposures to both sides of her neck and upper chest during this 13-year period.

Examination at the time of admission revealed an ulcerating lesion involving the entire right lateral wall of the hypopharynx, extending almost to the midline posteriorly. There were marked irradiation changes involving the skin of the neck bilaterally. No clinical evidence of metastatic cervical disease could be detected. Through an extra-oral approach a supraomohyoid neck dissection was performed with excision of the local intra-oral disease in continuity. It was necessary to utilize a split-thickness skin graft supported by tantalum mesh to close the defect. In February, 1954, the patient developed an independent primary focus high in the posterior wall of the pharynx just at the level of the soft palate, which on biopsy again proved to be squamous-cell carcinoma. This lesion was separated almost 2.5 cm. from its original primary and was, in our interpretation, a manifestation of the multicentric character of the disease process in her altered mucous membrane. Because of this feature of the disease process, the area was treated with the implantation of interstitial radon seeds in spite of the danger of extensive radionecrosis. The chance of total salvage seemed too remote to justify the morbidity and mortality of an adequate surgical procedure. Subsequently, the patient developed local recurrence in her right neck which involved and partially destroyed both the hyoid bone and thyroid cartilage. She refused laryngectomy and died of the disease on June 23, 1955.

CASE 5.—This man was 62 years old in November, 1953, when he presented himself for examination because of an ulcerating tumor mass in the left piriform sinus. He gave a history of having had treatment with external irradiation to both sides of his neck in 1919 because of a tuberculous lymphadenitis. The irradiation had produced the typical telangiectasia and thickened, indurated skin of the postirradiational type. He was admitted to the hospital, and a radical neck dissection and excision of the hypopharyngeal tumor was performed in continuity. Four months later further disease was apparent and he was readmitted to the hospital for consideration of total laryngectomy and pharyngeal reconstruction. This operation was not completed, however, because of involvement of the prevertebral fascia and anterior surfaces of the vertebral bodies. Palliative external x-irradiation was performed with some symptomatic relief. The patient died in November, 1954.

CASE 6.—In July, 1954, this 68-year-old retired contractor was seen for examination and treatment of a large, ulcerating mass involving the left side of the tongue, which produced considerable difficulty both in swallowing and articulation. His treatment history dated back 17 years, at which time a node was removed from the left jugular chain and was reported to be squamous-cell carcinoma, "anaplastic." The patient was treated with cross-fire irradiation through both sides of his neck and to the midline posteriorly, eliminating both the metastatic disease as well as what can now be postulated to have been nasopharyngeal primary tumor. He was well for 13 years until in 1950 he developed a lesion at the base of the tongue, extending into the tonsillar fossa, which was biopsied and found to be a squamous-cell carcinoma. The lesion appeared to be a localized one and initially was treated by transoral local excision. Some months later an operative procedure was performed on the left neck, removing two or three enlarged nodes, but no definitive neck dissection was undertaken. In 1952 a second transoral procedure was carried out, followed by a tracheostomy. This latter wound closed spontaneously, and from 1952 to 1954 the patient was relatively well, though gradually enlarging masses developed. No

treatment was undertaken for this disease. In March, 1954, while the patient was on a Southern vacation, an emergency tracheostomy was necessary. When he was first seen by us he suffered from dysphagia due to massive fixation of the tongue from recurrent tumor; his airway was completely obstructed at the base of the tongue and in the hypopharyngeal area. No definitive treatment seemed reasonable, and the patient was managed purely symptomatically.

These six patients all developed squamous-cell carcinomas of mucous membranes in areas treated by external x-irradiation from 9 to 25 years before appearance of the tumors. In each patient there was obvious late radiodermatitis in the skin utilized for the external port. There was also fibrosis of the tissues between the skin and the affected mucosa. There was microscopic evidence of radiation change in the mucosa and submucosa of all the cancer-bearing areas (Figs. 1-5). In no instance was treatment successful. We believe that, in part, this failure was due to multicentric origin of the tumors, with new foci developing in the irradiated mucosa at a rate which we were unable to control.

Three of these tumors, the two of the tongue and the one of the anus, developed in patients treated for cancer of adjacent organs or tissues. The anal lesion could hardly be a late localized recurrence of cancer of the cervix treated 11 years before; the one epidermoid carcinoma of the tongue could not be a recurrence of malignant mixed tumor of the parotid which showed no local persistence after 9 years. The other tongue lesion occurred in an irradiated area 13 years after successful radiotherapy for a presumed cancer of the nasopharynx. The two hypopharyngeal cancers occurred in patients treated for inflammatory cervical lesions, one of them tuberculous adenitis. The squamous-cell cancer of the buccal mucosa represents the culmination of a compound tragedy of errors in a patient whose ossifying fibroma of the upper maxilla was erroneously diagnosed as adamantinoma and treated with irradiation

Fig. 1 (Case 1).—Tissue near cancer of tongue showing hyperkeratosis, abnormal capillary dilatation, and hyalinization of vessel at 3 o'clock, all indicative of late irradiation effect.

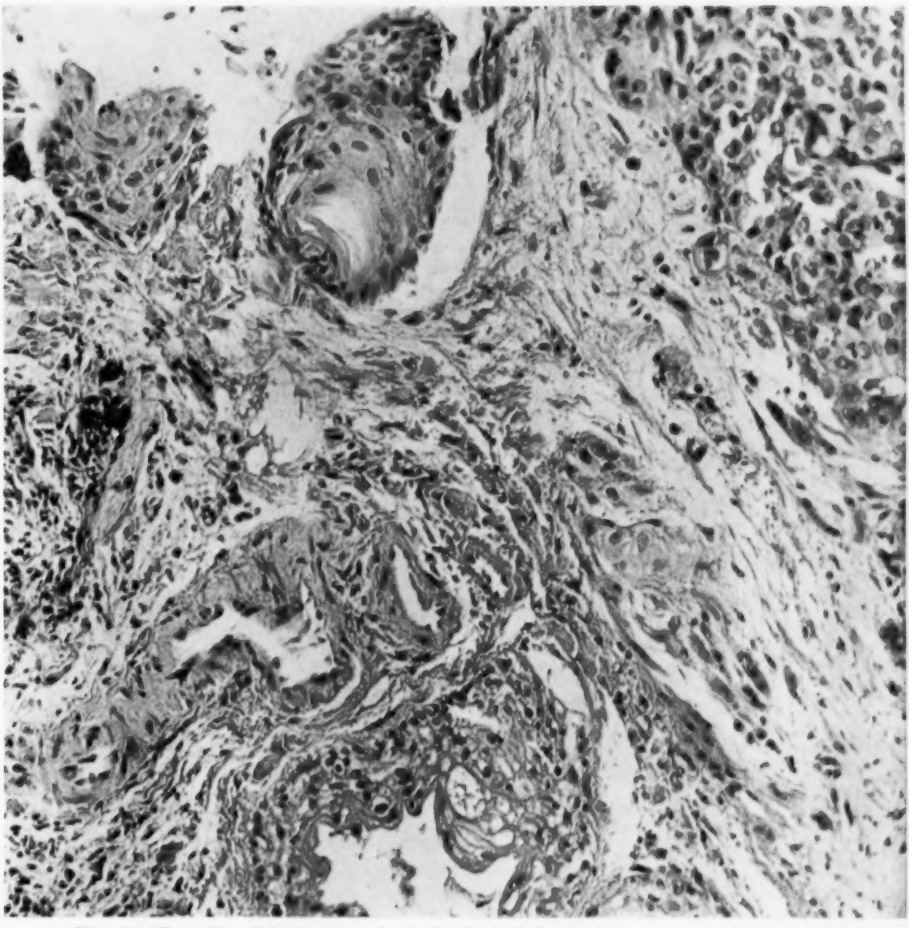


Fig. 2 (Case 3).—High-power view of edge of irradiation cancer of buccal mucosa, showing both keratinizing and undifferentiated epidermoid carcinoma in upper field, to left and right respectively, and arteriolar change consisting of intimal thickening, loss of elastica, and bizarre fibroblastic cells, characteristic of late irradiation effect.

over a period of years. Even if the tumor had been an adamantinoma the irradiation was incorrect treatment.

CASE 7.—A woman presented herself for examination in June, 1953, for closure of her colostomy. The patient had been in good health until June, 1950, when she experienced a severe episode of vaginal bleeding. She was hospitalized elsewhere, and a biopsy was taken from the uterine cervix which revealed a squamous-cell carcinoma. She was treated first with the application of radium, followed by external irradiation to four pelvic ports. In January, 1951, the patient developed a severe exacerbation of a residual radiation proctitis, necessitating the performance of a colostomy. This situation continued to the time of her first examination. The patient was hospitalized, and proctoscopic examination and barium studies of the distal loop revealed a perfectly patent lower bowel. There was an area of late radiation proctitis involving a segment of the anterior wall of the rectum for a distance of about 5 cm. An adequate lumen existed for a normal fecal stream, however.

The patient was prepared and operated upon with the intention of closing her colostomy. During the course of the operation, at the time of the examination of the distal loop of bowel, there was found a nodule in the low rectosig-

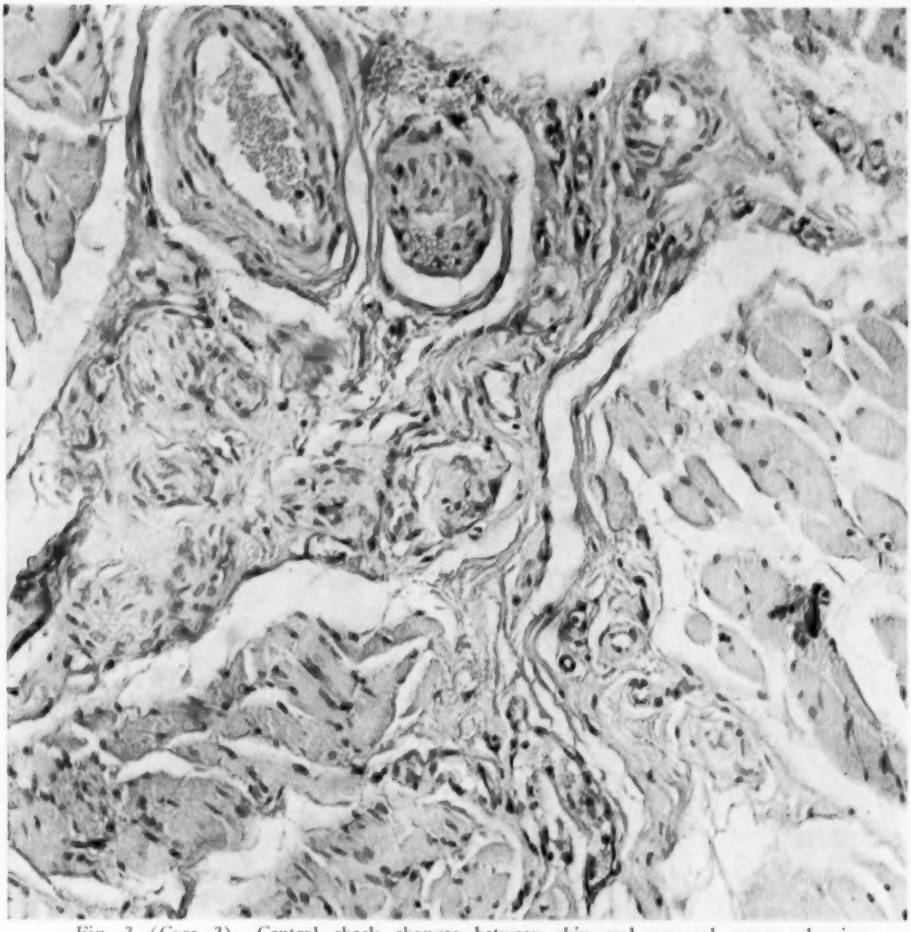


Fig. 3 (Case 3).—Central cheek changes between skin and mucosal cancer showing hyalinization of striated muscle and vessel changes of intimal proliferation, large bizarre cell formation, and obstruction of lumen, characteristic of late irradiation effect.

moid just above the peritoneal reflection within the indurated postradiational tissues, which caused some concern. A colotomy was performed adjacent to this mass, visualizing an ulcerated polypoid lesion which was obviously an early carcinoma. This distal segment of the bowel was excised and the colostomy closed through a primary anastomosis of the proximal loop and the distal one below the peritoneal reflection. The patient is living and well without evidence of disease from either of her primary sources almost three years following the second operation.

Case 8.—This 56-year-old business executive* was first seen in 1950, when he was admitted to the hospital because of cramping, lower abdominal pain of 6 week's duration. He had had a known duodenal ulcer for the previous 15 years, which was controlled by careful medical management. Annoyance with the modifications imposed on him by the dietary regimen, however, resulted in a change of management in 1946, four years prior to his hospital admission. At that time external irradiation was given over the mid-epigastrium in an effort to reduce the acid secretion of the stomach. Symptomatically the treatment was remarkably successful, since all ulcer symptoms disappeared. He discontinued his medical management and had been on a full and unrestricted

* Dr. Stuyvesant Butler has given permission to include this case in our series.

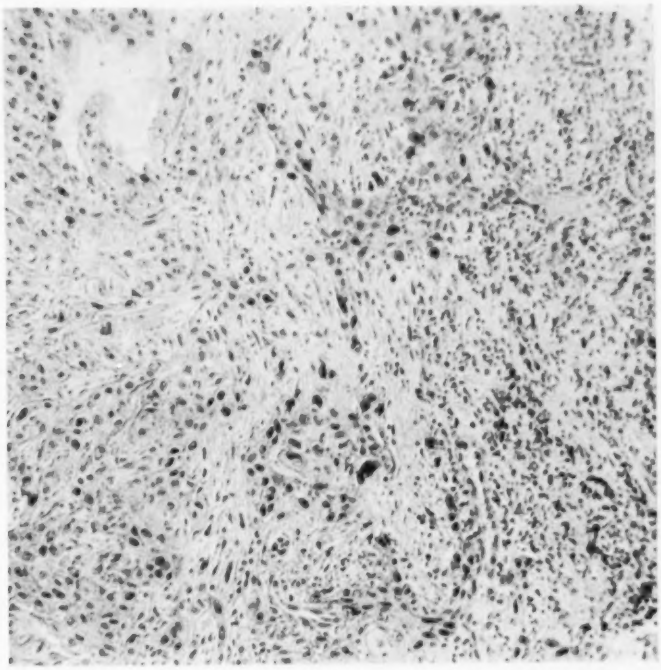


Fig. 4 (Case 5).—Epidermoid carcinoma of piriform sinus in area of pharynx medial to most marked irradiation change in skin of neck.

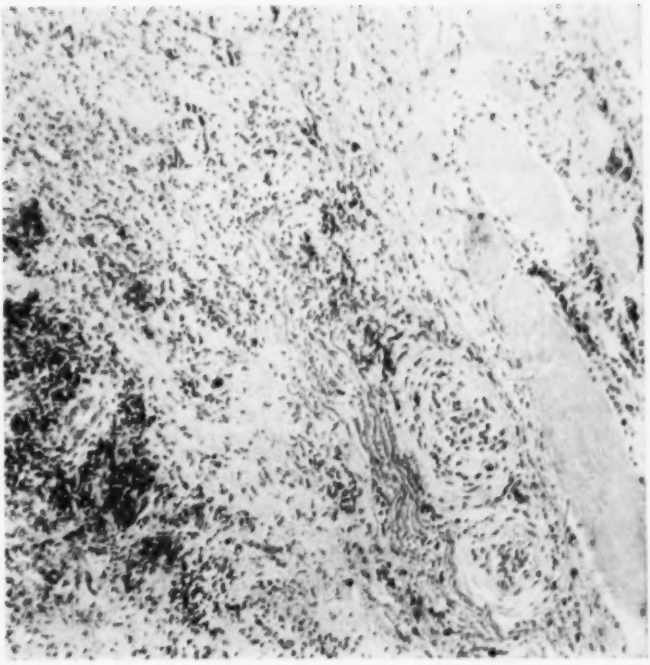


Fig. 5 (Case 5).—Base of hypopharyngeal cancer shown in Figure 4, exhibiting hyalinization of striated muscle, fibrosis, and virtual obliteration of arterioles with atypical fibroblastic proliferation.

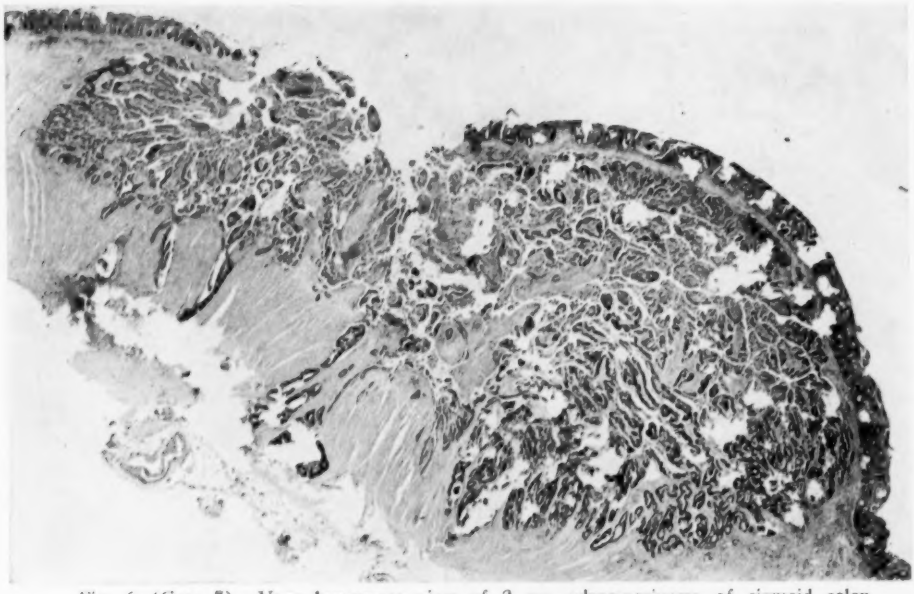
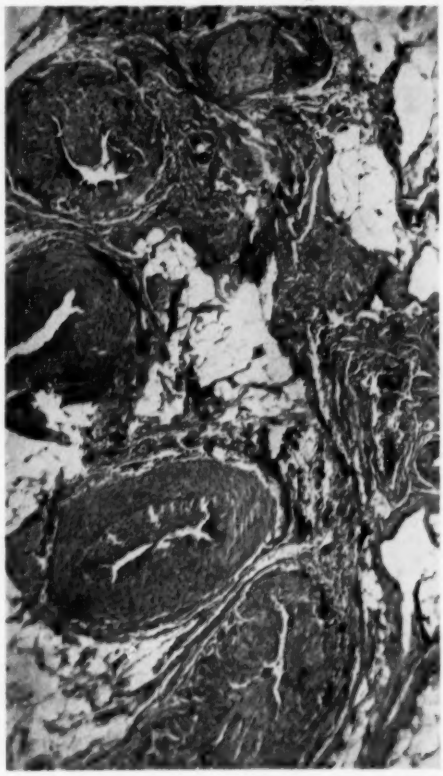


Fig. 6 (Case 7).—Very low-power view of 2 cm. adenocarcinoma of sigmoid colon found by accident in patient treated thirteen years previously by irradiation for epidermoid carcinoma of the uterine cervix.

diet until the onset of his present symptoms. A colon fluoroscopy was performed, which revealed a constriction of the transverse colon immediately beneath the field of the previous irradiation. The abdominal wall over the tumor revealed radiodermatitis and subcutaneous fibrosis. At the time of celiotomy a tumor mass was found in the mid portion of the transverse colon, which was resected and an end-to-end anastomosis performed. The tumor was an adenocarcinoma with metastases to the regional lymph nodes. Subsequently the patient developed hepatic metastases and died in December, 1952.

Case 9.—The patient was a 51-year-old ecclesiastical sister who was first seen in July, 1948, because of late radiation atrophy, dermatitis, and ulceration of the skin of her neck. In 1921, in Germany, she had received bilateral x-irradiation to her neck for "swollen glands," though the exact nature of the disease process is unknown. The irradiation change became apparent in the early 1940's and had been managed by various dermatologists with lubricating ointments. Excision and grafting of the damaged skin was finally performed on the left neck because of persistent ulceration. One year later the patient began to experience episodes of hematemesis for which she was hospitalized and a polyp of the cervical esophagus was removed locally. Microscopic examination of this tumor mass revealed adenocarcinoma in a pedunculated polyp without involvement of the stalk. The patient was well following

Fig. 7 (Case 7).—Arteriolar changes in submucosa and adventitia of irradiated bowel with small adenocarcinoma shown in Figure 6.



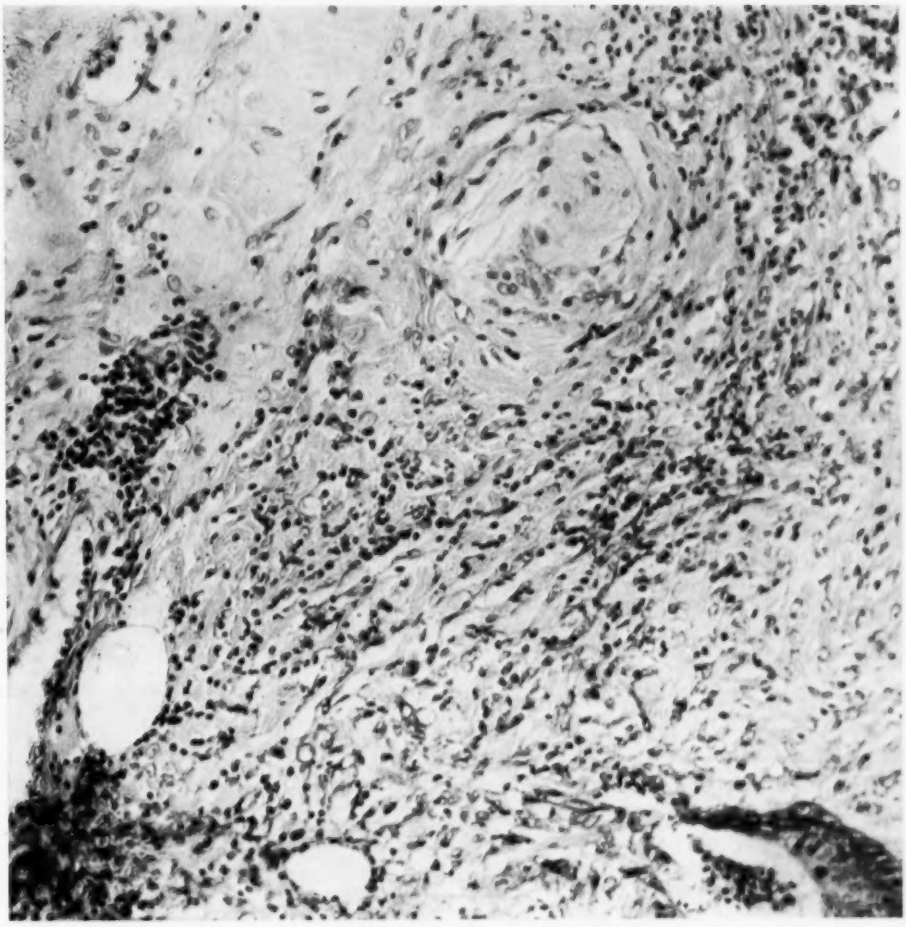


Fig. 8 (Case 8).—Low-power photomicrograph of edge of adenocarcinoma of transverse colon revealing aggregate of cancer cells at 5 o'clock, abnormally large and numerous capillaries, hyalinization and fibrosis of submucosa, and virtual obliteration of arteriolar vessels by intimal proliferation, all characteristic of irradiation effect.

this local procedure for almost two years when recurrence became apparent. She was hospitalized for consideration of laryngectomy and cervical esophagectomy. At the time of operation the lesion was inoperable because of fixation to the vertebral bodies and palliative management was instituted. Within the cervical esophagus there was diffuse adenocarcinoma, giving the impression of multicentric origin. The patient died in July, 1952.

These three instances of adenocarcinoma occurred in areas irradiated for other lesions. The adenocarcinoma of the transverse colon occurred directly beneath an obvious area of skin change on the anterior abdominal wall where irradiation had been used as treatment for a duodenal ulcer four years before. The time interval is short as compared with the intervals in reports of other irradiation-induced cancers, but the undeniable fact of the previous treatment and residual objective findings at least suggests itself as an etiological factor.

The carcinoma of the rectosigmoid occurred in the field of irradiation in a woman treated for cancer of the uterine cervix. Again the time interval is only three years, but there is demonstrable irradiation change

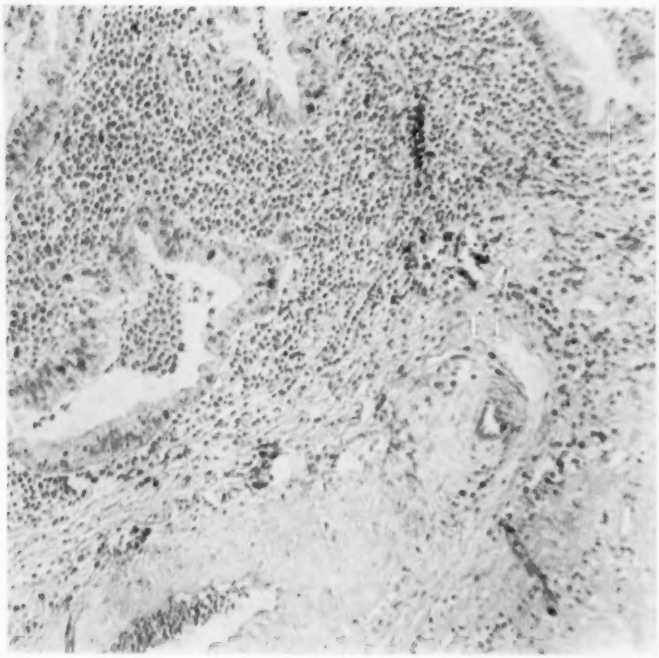


Fig. 9 (Case 9).—Adenocarcinoma of cervical esophagus in patient radiated 25 years before for probable cervical tuberculous adenitis. Arteriolar fibrosis and hyalinization of submucosa are apparent.

in the bowel wall about the tumor (Figs. 6 and 7).

The adenocarcinoma of the cervical esophagus is an extremely rare, but known, tumor. The long interval between irradiation and tumor formation (25 years) and the obvious irradiation changes in the tissues of the neck makes us believe that this is almost certainly an irradiation-induced cancer (Figs. 9 and 10).

Comment

The carcinogenic effect of irradiation has long been known, but the number of tissues susceptible is not generally appreciated. Skin cancer as a result of x- or gamma-irradiation is the most frequent and best documented entity. Martland's work on osteogenic sarcoma as a result of chronic radium poisoning is an example of the effect on bone of ionizing irradiation. Hatcher, Wilson and Brunschwig, Cahan et al., and Pettit have reported sarcomas of bone or soft parts subsequent to irradia-

Fig. 10 (Case 9).—Submucosal esophageal tissue revealing subintimal proliferation in vessels, hyalinization, and atypical and hyperchromatic fibroblasts characteristic of postirradiation fibromatosis.

tion. Relatively few studies have been made of carcinomas arising from mucous membranes, and of those reported all have been of squamous-cell type, occurring either in the hypopharynx and larynx, or adenocarcinomas of the uterine corpus. These uterine adenocarcinomas were all reported by Smith and Bowden from the Memorial Hospital series. The only other adenocarcinoma attributable to radiation (reported by Kindler in 1943) arose in the thyroid gland after irradiation for cervical tuberculous adenitis. Holinger has recorded two instances of squamous-cell carcinoma of the larynx and pharynx and one of fibrosarcoma of the larynx, which would appear to be irradiation-induced cancers occurring many years after radiotherapy of cervical tuberculous adenitis. His review of the literature, plus his own cases, revealed 11 reported instances of epidermoid cancer of the larynx and pharynx arising in areas irradiated many years before for tuberculosis or thyrotoxicosis. These reports, and the cases recorded here, are further evidence that the epithelium of mucous membranes, like that of the skin, is capable of malignant tumor formation as a late effect of irradiation.

Summary

Nine instances of irradiation-related carcinomas of mucous membranes are here reported. These tumors comprise six squamous-cell carcinomas, arising variously in the hypopharynx, the tongue, the buccal mucosa, and the anal canal, and three adenocarcinomas, two of the colon and one of the cervical esophagus.

30 N. Michigan Ave. (Dr. Southwick).

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Vertebral Nerve and Plexus

Components, Anatomical Relationships, and Surgical Implications

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The anatomical and functional relationships of the vertebral nerve as yet have not been clearly defined. In man, according to Van den Broek's [13] account, this nerve is formed by communicating rami derived from the sixth, seventh, and eighth cervical nerves. Potts [7] described it as a constant gray ramus associated chiefly with the seventh cervical nerve. According to his account, it extends rostrad along the medial surface of the vertebral artery and occasionally gives off branches to the eighth and the sixth cervical nerves. In one instance he observed a ramus coursing to the fifth cervical nerve. Potts' account is in general corroborated by that of Axford.[1] In a study of cervical sympathetic connections, Siwe [9] consistently found a stout ramus extending along the dorsal aspect of the vertebral artery which is connected by rami with the sixth and seventh cervical nerves. Independent of this ramus, he found one or more ventral rami, derived from the inferior cervical or stellate ganglion, that vary widely and communicate with several of the cervical nerves as well as with the middle cervical ganglion. He found no indication that these nerves contributed to the plexus on the vertebral artery, but he described the vertebral plexus on the subclavian artery and stated that it receives some twigs from the spinal nerves as they cross the dorsal arterial border. In a study of the communicating rami of the Rhesus monkey, Sheehan and Pick [8] consistently found the vertebral nerve connected by rami with the cervical nerves as far rostrad as the fourth. Skoog [10] found clumps of ganglion cells in the course of the vertebral nerve and described the origin of the nerve from the stellate ganglion. Christensen et al.,[3] studying the vertebral artery and nerve in the cat, found that the vertebral nerve conveys unmyelinated fibers to the cervical nerves from the eighth to the third. Upon removal of the inferior cervical or stellate ganglion the vertebral nerve underwent almost complete degeneration, but little or no visible change occurred in the plexus on the vertebral artery. Similar results were observed after removal of the entire cervical sympathetic trunk. In monkeys, according to Stilwell,[11] the vertebral plexus receives several communicating branches from the ventral surfaces of adjacent spinal ganglia and gives off rami to the anterior and posterior longitudinal ligaments, the vertebral periosteum, the dura mater, and the dorsal and ventral rami of the adjacent spinal nerves.

On the basis of the reported studies, it is apparent that there is no complete agreement relative to the true nature of the vertebral nerve and the vertebral plexus. Further investigation of the neural complex associated with the vertebral artery, consequently, is indicated.

Materials and Methods

Detailed dissection of the nerves related to the vertebral and basilar arteries and their connections was carried out bilaterally in a series of cadavers. Diagrams were made of the nerves in question before the removal of the tissues for histological study. Upon removal, these arteries and nerves were divided into pieces of which longitudinal sec-

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tions could be mounted on 3×1.5 in. slides. These longitudinal sections, cut at a thickness of 16μ to 20μ, were mounted serially and stained with hematoxylin and eosin. The sections were examined for ganglion cells, and the ganglia found were localized as accurately as possible on diagrams of the arteries. Counts of the ganglion cells in every ganglion were recorded.

Cross sections of the vertebral nerves and the rami connecting them with the cervical spinal nerves were prepared according to the Sudan black B method following postchroming. These sections were examined for myelinated fibers.

Anatomical Data

Vertebral Nerve and Plexus.—The rostral pole of the inferior cervical or stellate sympathetic trunk ganglion lies adjacent to the dorsal aspect of the junction of the vertebral and subclavian arteries. The intermediate cervical ganglion lies only a little farther rostrad on the ventral or ventromedial aspect of the vertebral artery. It is connected with the inferior cervical or stellate ganglion by two rami, one of which passes on either side of the vertebral artery.

In all of the 22 dissections carried out, nerves were traced from the inferior cervical or stellate and the intermediate cervical ganglion rostrad along the vertebral artery. Those derived from the inferior cervical or stellate ganglion, usually two or more, lie dorsal to the vertebral artery. As they extend rostrad most of their component fibers usually become incorporated in a single trunk which can be traced through the foramina transversaria to the level of the second or first cervical spinal nerve. Along its course this nerve is connected through slender rami with the cervical spinal nerves from the eighth to the second and probably the first (Fig. 1). It also gives rise to slender rami that take part in the formation of the plexus around the vertebral artery. In some instances most of the fibers that extend rostrad from the inferior cervical or stellate ganglion along the vertebral artery emerge from the ganglion in a single bundle. Occasionally slender rami also arise from the ansa vertebralis. The rami derived from the intermediate cervical

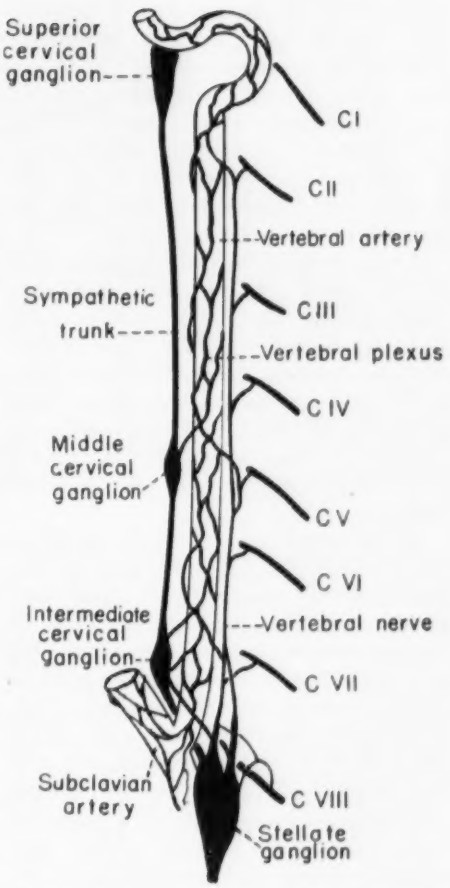

Fig. 1.—Diagrammatic illustration of vertebral nerve and plexus and their relationships to sympathetic trunk and cervical spinal nerves.

ganglion, usually two or more, that extend rostrad along the vertebral artery, lie ventral to the vessel for a short distance, and then break up into slender rami, some of which take part in the plexus formation around the artery and some join the vertebral nerve.

The neural plexus around the vertebral artery is continuous with the plexus on the subclavian artery, but relatively few of its constituent fibers appear to be derived from this source. It receives slender rami from cervical spinal nerves that can be demonstrated only with difficulty in gross dissections. The vertebral plexus is rela-

tively meager on the first part of the vertebral artery and becomes increasingly abundant as it extends rostrad. The vertebral nerve, on the other hand, becomes increasingly more slender as it extends rostrad because many fibers deviate from it in the rami through which it is connected with cervical spinal nerves and those that join the vertebral plexus.

At the level of the middle cervical sympathetic trunk ganglion several rami commonly extend from the sympathetic trunk into the prevertebral muscles. Most of these rami join cervical spinal nerves as sympathetic roots, but one or more usually joins the vertebral plexus. No rami could be traced from the superior cervical sympathetic trunk ganglion into the vertebral plexus.

At the rostral end of the vertebral artery the vertebral plexus is continuous with the plexus on the basilar artery. The latter plexus is made up predominantly of fibers derived from both vertebral plexuses, but it is less abundant than the middle portions of the vertebral plexuses. Subsidiary plexuses extend from the plexus on the basilar artery along its several branches.

Ganglia in Vertebral Nerve and Plexus

Microscopic examination of longitudinal serial sections of vertebral arteries and adjacent tissues has revealed numerous ganglia in both the vertebral nerves and the vertebral plexus. These ganglia are made up of multipolar ganglion cells comparable to those in the sympathetic trunk ganglia. In only 1 of 11 bodies in which the nerves associated with the vertebral arteries were examined for ganglia were none found in either the vertebral nerve or the vertebral plexus. Frequently, five or more ganglia were observed along a single vertebral artery. Ganglia may occur at any level along the vertebral arteries, but, as is apparent in Figure 2, more than 50% of those observed were located along the rostral half of the artery. The ganglia vary widely in size and in the numbers of their constituent ganglion cells. The lowest number of ganglion cells counted in a single ganglion is 7; the highest number is 24,708. The ganglion cell counts in most of the ganglia examined do not exceed 100, but ganglia that include 100 to 500 ganglion cells each occur frequently. Ganglia that include more than 1000 ganglion cells each occur only occasionally. A regular pattern of distribution of ganglia in the vertebral nerves and the vertebral plexus is not apparent. Their distribution in nerves associated with the right and left vertebral arteries in the same body is also asymmetrical. The approximate locations of the ganglia observed along the vertebral arteries in six bodies are illustrated diagrammatically in Figure 2. The adjacent numerals indicate the numbers of ganglion cells counted in every ganglion. Longitudinal serial sections of six basilar arteries and adjacent tissues revealed no ganglion cells in the nerves associated with this artery. In bodies in which the total number of ganglion cells in the neural complex associated with the vertebral arteries is relatively large, the vertebral plexus is more abundant than in bodies in which the total number of ganglion cells in these nerves is small. The axons of many of the ganglion cells in the vertebral nerve and plexus obviously ramify in the plexus. Those of others join cervical spinal nerves for their peripheral distribution.

Fibers of Vertebral Nerve and Rami to Spinal Nerves. — The rami that extend from the inferior cervical or stellate ganglion rostrad along the dorsal aspect of the vertebral artery and those that extend rostrad from the intermediate cervical ganglion are made up predominantly of unmyelinated fibers but also include numerous myelinated ones. In transverse sections of these rami taken near their origin from the ganglion, stained with Sudan black B, it is apparent that the myelinated fibers make up a larger percentage of the total number of fibers in some rami than in others (Fig. 3). Counts of the myelinated fibers in sections of some of the larger rami that extend from the stellate or inferior cervical gan-

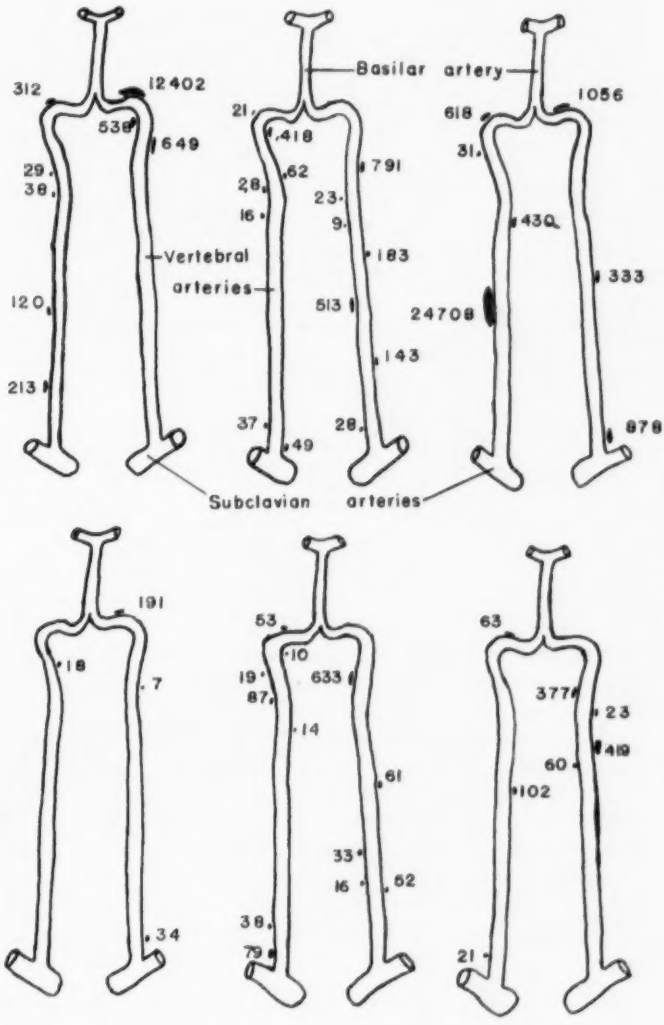

Fig. 2.—Diagrams of six pairs of vertebral arteries with approximate locations of ganglia in the vertebral nerve and plexus indicated in solid black. Adjacent numerals indicate ganglion cells counted in every ganglion.

glion into the vertebral nerve indicate totals in excess of 3000. The total number of myelinated fibers in the vertebral nerve in a given instance appears to be correlated with the total number of ganglion cells in the vertebral nerve and plexus. All but a very minor percentage of the myelinated fibers in the vertebral nerve are less than 4μ in diameter; consequently, they fall within the diameter range of preganglionic fibers.

Sections of the rami that connect the vertebral nerve with the cervical spinal nerves include myelinated fibers in lower percentages than the rami that unite to form the vertebral nerve. A limited number of counts of myelinated fibers in sections of these rami indicate an average of approximately 100 myelinated fibers in the one or more rami that join the successive cervical nerves, but the counts show relatively wide variation in the several cervical segments.

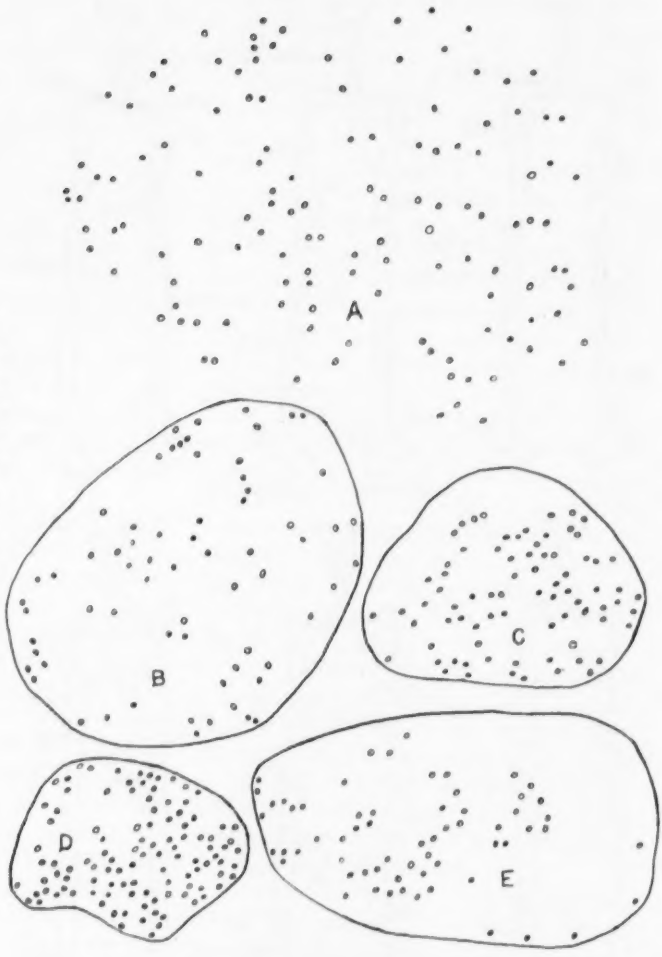

Fig. 3.—Drawings, with the aid of the camera lucida, from transverse sections of nerves stained with Sudan black B, to illustrate the density of myelinated fibers. *A*, selected area of a major root of the vertebral nerve extending from the stellate ganglion rostrad dorsal to the vertebral artery. *B*, *C*, *D*, and *E*, small rami extending from the intermediate cervical ganglion into the vertebral nerve and the vertebral plexus.

Some rami are made up almost exclusively of unmyelinated fibers (Fig. 4). All but a very minor percentage of the myelinated fibers fall within the diameter range of preganglionic fibers. Since these rami extend directly from the vertebral nerve to the cervical spinal nerves, they constitute conduction pathways from the sympathetic trunk to the cervical nerves that do not traverse regular sympathetic roots.

Comment

The data obtained in the present investigation support the assumption that the vertebral nerve is derived directly from the sympathetic trunk. It conveys fibers to the cervical spinal nerves and to the vertebral plexus. Since both the vertebral nerve and the vertebral plexus include ganglion cells, the vertebral nerve must convey preganglionic fibers to these cells. It is highly probable, therefore, that the myelinated vertebral nerve fibers, of which a high percentage falls within the diameter range of preganglionic fibers, are predominantly preganglionic. Most of them traverse thoracic communicating rami, but some emerge in the eighth cervical nerve and enter either

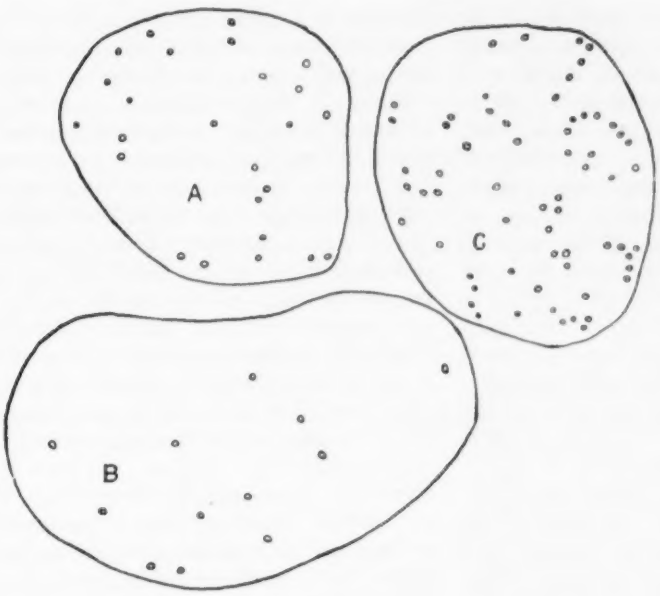

Fig. 4.—Drawings, with the aid of the camera lucida, from transverse sections of nerves stained with Sudan black B, to illustrate the density of myelinated fibers. *A* and *B*, rami that connect the vertebral nerve with a cervical spinal nerve. *C*, ramus from the middle cervical sympathetic trunk ganglion to the vertebral plexus.

the stellate or the intermediate cervical ganglion through communicating rami from this nerve. The unmyelinated vertebral nerve fibers undoubtedly are predominantly postganglionic. Since the rami through which the vertebral nerve is connected with the cervical spinal nerves, like the vertebral nerve, are made up predominantly of unmyelinated fibers and include myelinated ones that fall within the diameter range of preganglionic fibers, they undoubtedly convey both postganglionic and preganglionic fibers to the cervical nerves. The postganglionic fibers in these rami, like those of sympathetic roots, join the spinal nerves for peripheral distribution. The vertebral nerve with its rami, therefore, constitutes conduction pathways from the sympathetic trunk to the cervical nerves that do not traverse regular sympathetic roots. Some of the preganglionic fibers in question probably join the cervical sympathetic trunk. Others probably terminate in accessory cervical sympathetic ganglia. In addition to the preganglionic fibers that terminate in ganglia in the vertebral plexus, this plexus also receives postganglionic fibers through the vertebral nerve. The fibers derived from the plexus on the subclavian artery and those derived from the middle cervical sympathetic trunk ganglion probably make up only a minor portion of the vertebral plexus.

As has been demonstrated in monkeys,[11] cervical spinal nerve fibers join the vertebral plexus to be distributed through branches that arise from it to the anterior and posterior ligaments, the vertebral periosteum, other tissues related to the vertebrae, and the dura mater. A comparable distribution of cervical nerve fibers through the vertebral plexus undoubtedly obtains in man. The fibers in question are predominantly afferent, and many of them are myelinated. The small numbers of myelinated fibers that are larger than preganglionic fibers and some that fall within the diameter range of preganglionic fibers in the rami that connect the vertebral nerve with the cervical spinal nerves undoubtedly are afferent. The remaining myelinated fibers in these rami can readily be accounted for as preganglionic.

In view of their constituent fibers and their anatomical relationships, the vertebral nerve and the rami through which it is connected with the cervical spinal nerves may be compared with sympathetic roots that include, in addition to postganglionic fibers, relatively large numbers of preganglionic ones and a small percentage of afferent fibers. In view of the ganglion cells located in this nerve and in the vertebral plexus that are synaptically related to preganglionic vertebral nerve fibers, the vertebral nerve cannot be regarded merely as a conduction pathway, but it represents a neural structure that includes synaptic relays. In this respect it is comparable to the splanchnic nerves.[12,4]

The vertebral plexus is essentially a perivascular neural plexus. In view of the presence in it of numerous ganglion cells, it is similar to the neural plexuses on the mesenteric arteries.[6] It includes both pre- and postganglionic sympathetic and some afferent fibers. Like the splanchnic periarterial plexuses, it also includes synaptic relays.

As has been demonstrated in the cat,[3] interruption of the vertebral nerves by extirpation of the inferior cervical or stellate ganglion or the entire cervical portion of the sympathetic trunk results in complete degeneration of the vertebral nerve but the vertebral plexus undergoes no apparent degeneration. This undoubtedly can be explained most satisfactorily on the basis of the continuity of the vertebral plexus with the plexus on the subclavian artery and the presence in the vertebral nerve and the vertebral plexus of numerous ganglion cells. The fibers derived from the ganglion cells in the vertebral plexus contribute largely to its fiber components. The increasing abundance of the vertebral plexus from the origin of the vertebral artery rostrad can readily be explained on this basis. Degeneration of the fibers of the vertebral nerve that are interrupted by cervicothoracic sympathectomy need not be apparent in the vertebral plexus, since the fibers in this category that become incorporated in it enter the plexus in small bundles and constitute only a minor portion of its fibers.

From the surgical point of view it is evident that complete sympathetic denervation of the upper extremity and the cervical and cephalic regions cannot be achieved without interruption of the vertebral nerve, since it conveys fibers that form conduction pathways from the sympathetic trunk to the cervical spinal nerves that do not traverse sympathetic roots that arise directly from the sympathetic trunk. Since this nerve is made up predominantly of postganglionic fibers that arise in the inferior or stellate ganglion and preganglionic fibers that traverse this ganglion, most of its fibers are interrupted by inferior cervical or stellate ganglionectomy. Conduction through the vertebral nerve and the sympathetic roots that arise from the intermediate cervical ganglion, however, is not in all cases abolished by removal of the inferior cervical or stellate ganglion, since the intermediate cervical ganglion, at least in many instances, receives preganglionic fibers directly through a communicating ramus from the eighth cervical nerve. The occurrence of preganglionic fibers in the ventral root of the eighth cervical nerve has been demonstrated in man both experimentally[2] and anatomically.[5] In the experiments of Bridges and Yahr[2] vasoconstriction in the homolateral digits elicited by electrical stimulation of the ventral root of the eighth cervical nerve was demonstrated plethysmographically in a series of patients. Some of the preganglionic fibers concerned reach the intermediate cervical ganglion directly from the ventral root of the eighth cervical nerve. In patients in whom preganglionic fibers reach the intermediate cervical ganglion without traversing the inferior cervical or stellate ganglion, complete sympathetic denervation of the upper extremity and the cervical and cephalic regions obviously cannot be achieved surgically without section of these fibers or extirpation of the intermediate cervical ganglion. Some failures

to achieve complete cervical sympathetic denervation by cervicothoracic sympathectomy undoubtedly can be explained on the assumption that preganglionic fibers to the intermediate cervical ganglion remained intact. The postganglionic fibers in question reach the cervical nerves in part through direct sympathetic roots from the intermediate cervical ganglion and in part through the vertebral nerve and its rami and are widely distributed in the areas innervated through the cervical nerves. Extirpation of the intermediate cervical ganglion in addition to cervicothoracic sympathectomy as it is usually carried out, therefore, would be advantageous in many patients.

Extirpation of the superior cervical ganglion or the entire cervical portion of the sympathetic trunk rostral to the intermediate cervical ganglion leaves the vertebral nerve essentially intact. Superior cervical sympathectomy, consequently, does not insure complete sympathectomy of any of the cervical segments nor does it insure complete interruption of the cephalic sympathetic nerves.

Summary

The vertebral nerve is derived predominantly through rami that arise from the inferior cervical or stellate ganglion. Lesser rami arise from the intermediate cervical ganglion. The nerve lies dorsal to the vertebral artery and extends rostrad to the level of the second or first cervical nerve. It is connected through slender rami with the cervical spinal nerves from the eighth to the second or first, and contributes rami to the vertebral plexus. Both the vertebral nerve and the vertebral plexus include ganglia that receive preganglionic fibers through the vertebral nerve, but this nerve is made up predominantly of postganglionic fibers. Many postganglionic and some preganglionic fibers reach the cervical spinal nerves through the rami that connect them with the vertebral nerve. Complete surgical sympathetic denervation of the upper extremity and the cervical and cephalic regions, therefore, cannot be achieved without interruption of the vertebral nerve. The surgical implications of this nerve and the intermediate cervical ganglion are considered.

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Giant Neurofibroma of Mesentery

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Solitary benign neurofibromas of the abdominal cavity may achieve gigantic proportions before coming to the attention of the surgeon, who is then faced with the difficult task of treatment. Such tumors are, fortunately, rare, and have been mentioned in the medical literature only on infrequent occasions.

It is generally accepted that these lesions represent a manifestation of von Recklinghausen's disease, and in most reported cases there is evidence of more widespread distribution in the form of cutaneous and other visceral nodules. The case presented in this report is unusual in that the tumor was of huge size and apparently solitary, no other stigmata of von Recklinghausen's disease having been so far discovered.

Report of a Case

A 22-year-old man was referred to hospital on Sept. 26, 1951, with a noticeable abdominal mass of three weeks' duration. This was associated with a vague, generalized, aching pain in the lower abdomen, also of three weeks' duration. The pain was not severe enough to prevent him from working but was probably responsible for his finding the abdominal mass. There were no accompanying gastrointestinal disturbances, nausea, vomiting, or diarrhea, and otherwise he felt in excellent health.

His past history reveals only the usual childhood diseases, and, at the age of 2½ years, a bilateral herniorrhaphy.

Physical examination on admission showed a healthy young man of 22 years. The head, mouth, neck, respiratory system, and cardiovascular system were entirely normal. Blood pressure was 160/60; pulse rate, 90 per minute. Abdominal examination revealed a smooth rounded firm slightly movable mass, measuring approximately 10 cm. in diameter in the right lower quadrant. The upper and lower extremities and genitalia were normal.

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Laboratory investigation revealed a hemoglobin value of 17 gm., hematocrit value of 46%, WBC 11,900, with neutrophils 78%, lymphocytes 20%, and monocytes 2%. Urinalysis: chemical and microscopic examination showed no abnormalities. Wassermann test was negative. Total serum proteins, 5.3 gm. per 100 cc.—albumin 2.9 gm., globulin 2.4 gm. Sedimentation rate, 2 mm. in an hour.

It was decided to investigate the mass by laparotomy. This was done, and the surgeon's report states that "a huge mass was found involving the mesentery of the small intestine." Several biopsy specimens were taken. Pathological report: "Gross examination showed numerous fragments of firm, white, homogeneous tissue. Microscopic diagnosis: fibroma of mesentery."

The patient's postoperative course was uneventful, and he was discharged from hospital. He was readmitted on Oct. 17, 1951, for a more definitive treatment. His complaints remained solely confined to his abdomen. All findings on physical examination, with the exception of the abdomen, were normal. Reexamination of the abdomen revealed a firm round mass now located approximately beneath the umbilicus and measuring 12 cm. in diameter. In addition, there was a smaller soft elongated mass in the right lower quadrant measuring 10×3 cm. Laboratory investigation revealed a hemoglobin value of 14.7 gm., hematocrit value of 38%, WBC 6400 with neutrophils 68%, sedimentation rate 1 mm. in an hour. Urinalysis was negative; examination of stool for occult blood showed 3+ reaction. On Oct. 20, 1951, a surgical resection was undertaken and the mass was removed with considerable difficulty.

Pathological Report.—Gross Examination: Specimen consisted of 140 cm. of ileum measuring from 4 to 5 cm. in diameter. Occupying the mesentery of a larger part of the ileum was a firm flat, pancake-like tumor measuring 24×11×4 cm. (Fig. 1). Its surface was yellowish-gray and nodular, and it was covered with congested venous channels. The tumor was largely confined to the mesentery, although in a few areas it extended onto the serosal surface of the ileum in the form of small seed-like nodules and also extended into the root of the mesentery. On section, the mass was seen to be composed of discrete spherical and ovoid nodules varying from several millimeters to 1 cm. in diameter, pearl-gray and firm. These nodules

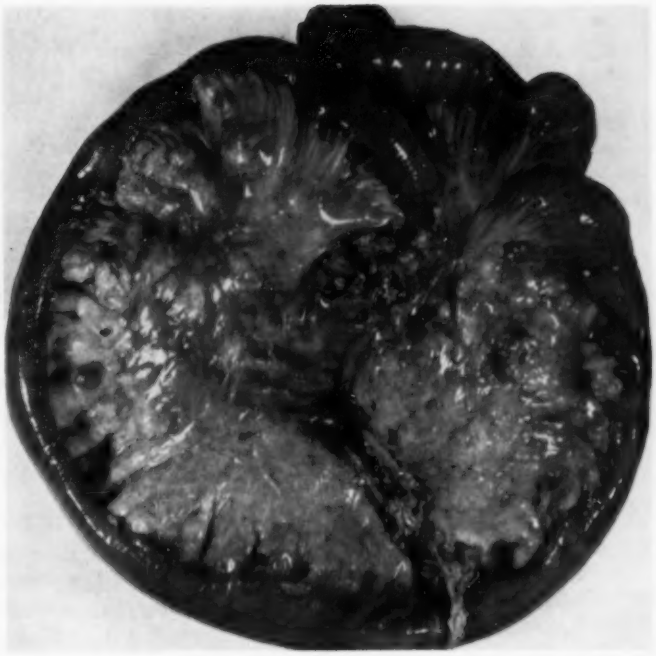

Fig. 1.—Plexiform neurofibroma of mesentary, approximately one-third natural size.

were separated by a loose gray stringy connective tissue in which remnants of mesenteric fat could be seen. The tumor did not penetrate the wall of the ileum in any location.

Microscopic Examination: Sections showed typical plexiform neurofibroma, consisting of variably sized round and ovoid nodules separated by a coarse collagenous connective tissue containing blood vessels (Figs. 2 and 3). Each nodule was composed of wavy bundles of fusiform cells separated by varying amounts of loose stroma in which there were areas of mucoid degeneration. The cells were of fairly uniform size and shape and moderately sparse in distribution. No areas of excessive cellularity or pleomorphism were noted.

Diagnosis: plexiform neurofibroma of mesentery.

Follow-Up Reports.—June 25, 1954, the patient was entirely well. Physical examination, chest

Fig. 2.—Neurofibroma of mesentery; the characteristic lobulated pattern is seen clearly. Hematoxylin and eosin; ×7.

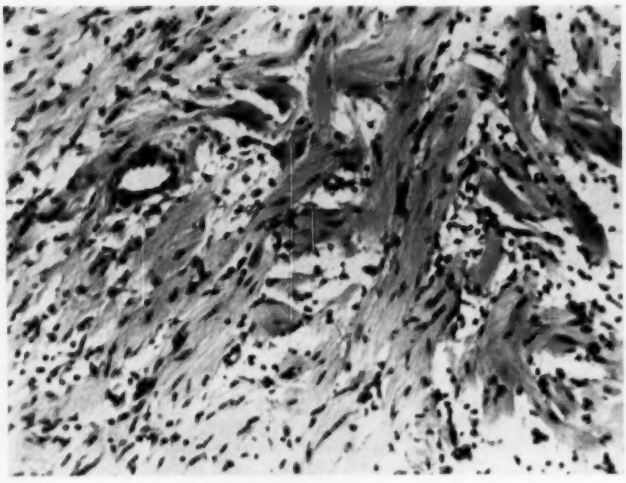

Fig. 3.—Neurofibroma of mesentery. High magnification reveals interlacing wavy bundles of fusiform cells of only slightly variable character. Hematoxylin and eosin; × 135.

x-ray, and barium meal follow-through showed no abnormalities.

On Feb. 8, 1956, the patient remained perfectly well. Physical examination was still entirely normal.

Comment

It is apparent from a survey of the literature that the majority of cases of visceral neurofibromatosis are accompanied by other manifestations of von Recklinghausen's disease in the form of variable numbers of cutaneous and visceral nodules. Further, in most of the abdominal neurofibromatoses, the tumor appears to arise from, and principally involve, the intestinal tract, mainly the ileum,[1-6,9] although the stomach [8] and colon [7,12] are occasionally mentioned as sites of origin. Involvement of the mesentery only is mentioned in one report [10] and the greater omentum in another,[11] and in both of these there were manifestations of more widespread disease.

The case reported here appeared to involve the mesentery of the small intestine only, with spread to the ileum occurring secondarily by direct continuity. The tumor extended to the root of the mesentery, rendering complete removal difficult. Despite this, there has been no recurrence of the tumor over nearly five years, as indicated by the follow-up reports.

Histologically the tumor was a typical plexiform neurofibroma of benign appearance, with no evidence of active growth in numerous sections studied. This appearance belied the initial gross impression of sarcoma suggested by the size and the presence of small tumor nodules extending onto the serosal surface of the encircling ileum. Such appearances rendered the immediate accurate surgical diagnosis of the tumor difficult, especially since no other stigmata of von Recklinghausen's disease were present.

Establishment of a correct diagnosis is important, since complete surgical removal will usually result in a cure. If removal is incomplete, recurrence is probable, together with the possibility of malignant degeneration, which is stated to occur in about 13% of these tumors.[13,14] Search should also be made for additional manifestations of von Recklinghausen's disease, since malignant change may also occur in one of these at a later date.

Summary

A case of giant neurofibroma of the mesentery with a five-year cure is presented. A brief review of the literature reveals that the occurrence of such a large solitary lesion is rare and that, in most instances, other stigmata of von Recklinghausen's disease are present.

Addendum

A recent communication received from the Alberta Cancer Clinic, Edmonton, Alta. dated Feb. 6, 1957, contains the following information. "Further investigation of the patient reveals multiple variously-sized, cafe-au-lait spots over the back and trunk and to a less extent on the extremities. Soft, bluish intradermal lesions are scattered over the back, shoulders and left thigh. There is no evidence of recurrence of the intra-abdominal tumour."

The Edmonton Clinic, Division of Cancer Services, Province of Alberta, Canada, provided the follow-up studies.

The Vancouver General Hospital, Department of Pathology (9).

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One-Stage Retrosternal Esophagoplasty Using Right Side of Colon

Report of a Case of Late Reconstruction in Congenital Esophageal Atresia

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In esophageal atresia the treatment of choice usually includes primary anastomosis of the esophageal segments. However, in some patients the distance to be bridged is so great that primary anastomosis may be dangerous or impossible. When such a situation exists, the surgeon may choose to perform cervical esophagostomy and tube gastrostomy and defer esophageal reconstruction to a later date.

Esophageal replacement has been accomplished by utilizing stomach,[1-3] jejunum,[4-6] and skin tubes.[7] Although the stomach can be mobilized adequately to permit its anastomosis to the cervical esophagus, an intrathoracic position may cause complications. Some of the more commonly reported complications following this procedure are chronic gastritis, esophagitis, stricture of the suture line, nausea, and, occasionally, respiratory disorders.

The use of jejunum in esophagoplasty has been investigated by Yudin,[8] Longmire,[9] Mes,[10] and others. In this procedure the cardinal difficulty is centered about the jejunal vascular supply, which can be extremely delicate and susceptible to injury. The incidence of failure from vascular catastrophe has been high. Even when such a jejunal graft succeeds, ulceration from gastric and intestinal secretions can be a serious problem. To avert peptic jejunitis, some surgeons have elected to bypass the stomach, a procedure which can lead to nutritional and metabolic deficiencies, particularly in the newborn infant.

Multiple-stage procedures for building an antethoracic esophagus are being abandoned.[11] The high incidence of stricture and fistula, the poor cosmetic appearance, and the long periods of hospitalization are the principal disadvantages in this method of repair.

Use of the colon for esophagoplasty was suggested to us by a report from Dale and Sherman,[12] who successfully treated the esophageal atresia of two patients in such a manner. Although various antethoracic substitution procedures using the colon had been reported since the early 1900's, the study of Dale and Sherman is the first we could find which deals with intrathoracic colon transplant for correction of esophageal atresia.

Report of a Case

A 2-day-old girl was admitted to Doernbecher Memorial Hospital for Children on July 3, 1953, because of a congenital tracheoesophageal fistula, Type III.

She was taken to the operating room the same day. After the lesion was exposed through a right-sided transpleural incision, it was seen that the upper segment of the esophagus ended in a blind pouch high in the mediastinum. The lower segment was attached to the trachea at the carina, where it formed a fistulous communication.

After the lower segment was detached from the trachea and the trachea was closed, an attempt was made to bring the upper and lower

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portions of the esophagus together for end-to-end anastomosis. Even though the upper segment had been freed for a considerable distance into the neck and the lower segment had been faced toward the diaphragm, there remained a gap of 1.5 cm. between the two segments. Therefore the proximal end of the distal segment was closed and the distal end of the upper segment was brought out through the left side of the neck for a temporary esophagostomy. A tube gastrostomy was also performed.

The patient made a good recovery and was discharged from the hospital. Gastrostomy feedings were continued for two years, during which time she remained in good health.

On July 27, 1955, she was readmitted to the hospital for establishment of esophagogastric continuity. At this time she weighed 12 kg. (26½ lb.) and was in excellent physical condition. X-ray examination of the colon demonstrated a normally rotated cecum and an ascending colon of normal length.

Preparation for operation was carried out as suggested by Dale and Sherman.[18] This consisted of succinylsulfathiazole by gastrostomy tube, 1 gm. three times daily; magnesia magma (milk of magnesia), 15 cc. by gastrostomy tube at bedtime, and a tap-water enema daily. Sixty hours before operation, neomycin was also started, by gastrostomy tube, 0.5 gm. being administered every hour for four doses and then every four hours until the morning of the operation. At that time 300,000 units of aqueous penicillin was given intramuscularly.

The reconstruction operation was performed on Aug. 1 with general endotracheal anesthesia. The abdomen was opened through an upper right paramedian incision. Exploration of the abdominal cavity revealed no congenital anomalies or other abnormalities. The cecum, ascending colon, and hepatic flexure were mobilized by dividing the lateral peritoneal attachments. The right colic artery was then occluded with a bulldog clamp to test the collateral circulation to the cecum. During this testing interval an appendectomy was performed. The circulation to the cecum and ascending colon was not embarrassed. The color of the bowel and mesentery remained normal, and the pulsation of the small arteries on the bowel wall could still be seen.

The right colic artery was then divided and ligated (Fig. 1). The ileum was transected about 2.5 cm. from the ileocecal valve, the distal end being inverted and closed. After it was made certain that the mobilized colon had sufficient length to permit anastomosis to the cervical esophagus, the transverse colon was divided distal to the middle colic vessels (Fig. 2). The ileum was anastomosed end-to-end to the distal segment of the transverse colon. A tunnel was then created in the anterior mediastinum, immediately posterior to the sternum.

A low transverse neck incision was made, surrounding the esophagostomy. The mediastinal dissection was facilitated by working simultaneously through both neck and abdominal incisions. This dissection was not difficult, much of it being done under direct vision and most of it being carried out with blunt instruments and the finger. The cecum and ascending colon were then passed through the tunnel, the cecum being brought into the neck. When the wall of the cecum had been incised, the usual amount of bleeding took place, which demonstrated again that there was adequate collateral circulation through the middle colic vessels.

A two-layer anastomosis was carried out easily and without tension between the esophagus and cecum, using interrupted 0000 nonabsorbable surgical (chromic and Deknatel silk) sutures. Following closure of the neck incision, the transplanted segment of colon was anastomosed to the anterior wall of the stomach (inset, Fig. 2). The abdomen was closed, and the patient was returned to her room in good condition. Auscultation of the chest and a roentgenogram of the chest, taken with a portable machine, revealed both lungs to be fully expanded and no evidence of pneumothorax.

On the second postoperative day small feedings of 5% dextrose in isotonic saline were started through the gastrostomy. These feedings were gradually increased in amount and strength by the addition of skim milk. By the fourth postoperative day the patient was tolerating her preoperative gastrostomy formula. There was no postoperative morbidity. Fluids were offered orally and taken slowly in small amounts on the seventh postoperative day. The patient was discharged on the 15th hospital day (9th postoperative day).

After returning home, the patient regurgitated frequently. Fluoroscopy disclosed that swallowed barium went easily and immediately into the cecum and continued through the colon to below the level of the diaphragm. But the barium entered the stomach slowly, and a fluid level could be seen in the retrosternal colon. Gradually this situation improved. On Sept. 9 (40 days postoperatively) the gastrostomy feedings were discontinued entirely. X-ray studies of the upper gastrointestinal tract on Sept. 19 showed good progress of the swallowed barium into and through the new esophagus and into the stomach (Fig. 3, *A* and *B*).

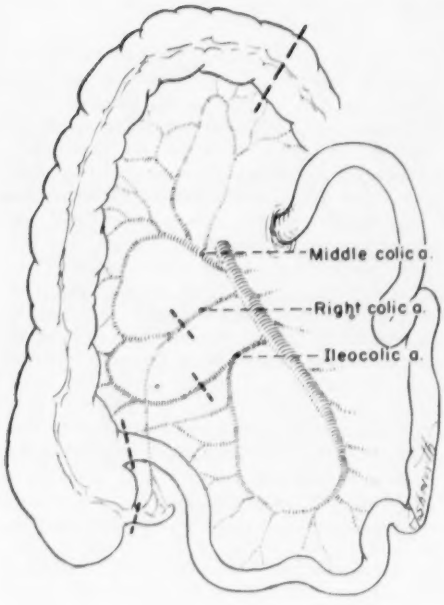

Fig. 1.—Schematic drawing illustrating sites for division of the ileum, colon, and right colic artery.

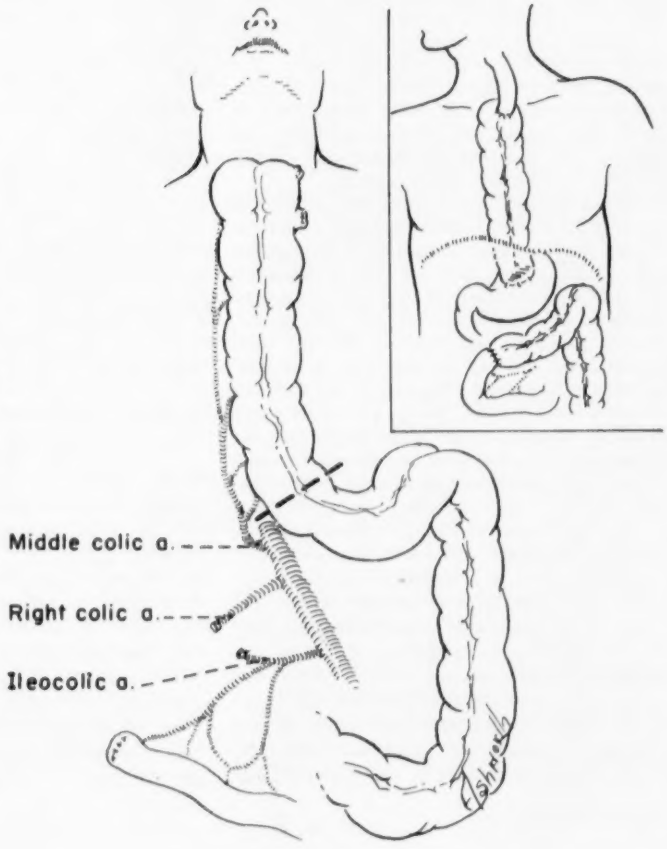

Fig. 2.—Schematic drawing showing that the cecum with its blood supply intact can be brought to the neck. Inset, completed anastomosis.

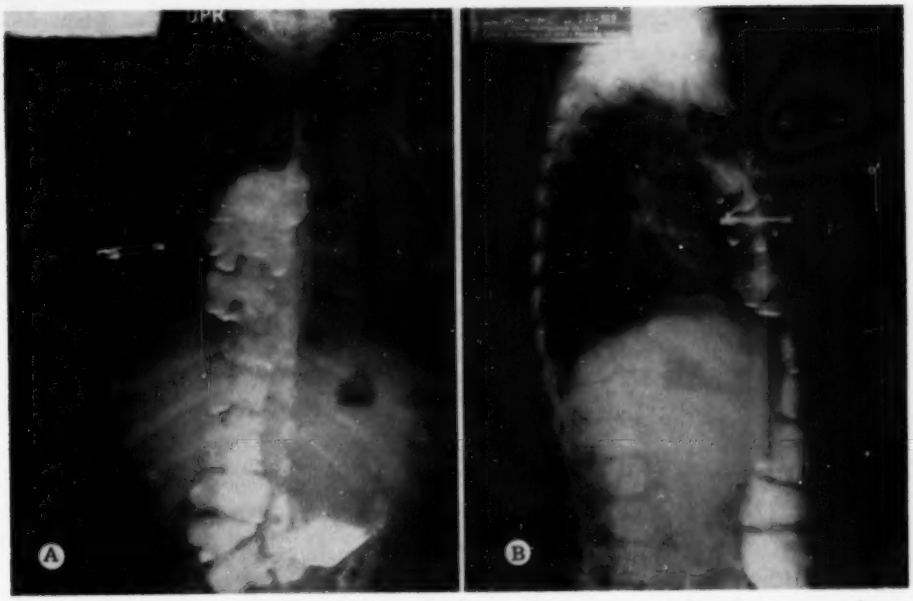

Fig. 3.—*A*, anteroposterior, and *B*, lateral, views of upper gastrointestinal tract made on Sept. 19, 1955. Note barium in retrosternal segment of colon and in stomach.

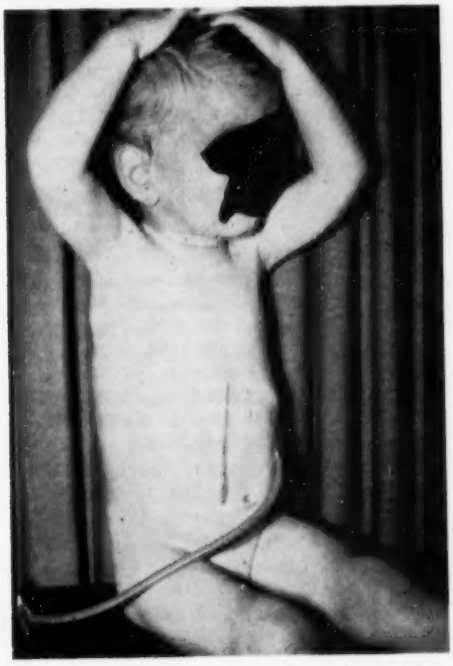

Fig. 4.—Appearance of patient in October, 1955. Gastrostomy tube still in place, but all feedings being taken orally.

On Oct. 3 the mother reported that the patient was eating a diet normal for her age. Occasionally she would regurgitate if the food was not finely divided. However, she could stand on her head without regurgitating.

On Oct. 5, and again on Oct. 12, esophagoscopy was performed. The stoma was visualized, and dilators, through size 22 F., were passed without meeting any significant resistance. We planned to continue the dilatations, but the child has done so well there seems to be no necessity to do so. Figure 4 shows the appearance of the child in October, 1955.

On Nov. 12 the gastrostomy tube came out accidentally. It has not been replaced.

Comment

Through the years esophageal substitution has remained a most difficult surgical problem. At the Doernbecher Memorial Hospital for Children our experience with the use of stomach or jejunum in esophagoplasty has been disappointing. Recurrent strictures, persistent fistulas, and vascular catastrophies have been common. Therefore, the new procedure described by Dale and Sherman [12] was of particular interest to us.

The advantages of colon substitution over other methods in esophagoplasty are impressive. Battersby [13] demonstrated not only that the length of the mobilized colon is adequate for anastomosis without tension but also that the vascular supply is superior to that of mobilized jejunum. Therefore, complications such as fistula or stenosis should be less frequent when colon is used.

Another decided advantage seems to be the increased resistance of the colonic mucosa to ulceration by gastric secretions, as demonstrated by Wangensteen [14] and Moroney [15] and others. Furthermore, retrosternal placement of the substituted esophagus gives an almost perfect cosmetic result in contrast to the unsightly appearance of antethoracic placement.

The most obvious advantages are that it permits a one-stage procedure and requires a short period of hospitalization.

Our experience with the case here reported has impressed us favorably not only with regard to the technical aspects of the operation but also with regard to the excellent anatomic and physiologic condition of the patient postoperatively.

Summary

In certain cases of congenital atresia of the esophagus a primary end-to-end repair may be impossible or unwise. Cervical esophagostomy and feeding gastrostomy may be safer, deferring esophagoplasty to a later date.

In the formation of a substitute for the thoracic esophagus the use of a portion of the colon has several advantages. The most important are that it allows a one-stage procedure and requires a short period of hospitalization.

A case is reported in which the right side of the colon was brought up through a retrosternal tunnel and used to bridge the gap between cervical esophagus and stomach.

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Observations Based on Two Hundred Forty-Five Consecutive Gastrectomies for Duodenal Ulcer Disease at Brooke Army Hospital

Comparison of Two Groups of Billroth II Gastrectomies

LIEUT. COL. J. F. SCHIRMER (MC), and COL. WARNER F. BOWERS (MC), U. S. Army

Introduction

Years of experience and clinical investigation into the cause of duodenal ulcer and the results of treatment have resulted in some general agreement as to factors involved in the pathogenesis of the ulcer and the general methods of management of patients. With respect to the technical aspects of surgical operations designed to cure duodenal ulcer, however, there remains a wide diversity of opinion. There are advocates of Billroth I and Billroth II types of operation, large- or small-stoma, vagotomy with or without gastroenterostomy, antecolic or retrocolic anastomosis, and recently even a proponent of staged procedures for treatment of the disease beginning with gastroenterostomy as a preliminary procedure.[1]

True comparisons between the end-results of operations which are technically different, but performed on the same general type of patient population by surgeons with similar equipment and treatment facilities, are not often reported. This analysis is thought to be of value in that regard.

This study is concerned with the results of 245 consecutive subtotal gastrectomies for duodenal ulcer during the period 1949 to 1954 at Brooke Army Hospital. During half this time the operations performed consisted of 75% resection of the stomach with restoration of gastrointestinal continuity by a retrocolic, no-loop, narrow-stoma, end-to-side gastrojejunostomy. This operation will be referred to, herein, as the "advocated operation." During the earlier part of this study the operation consisted of resection of about 60% of the stomach, restoration of gastrointestinal continuity being accomplished by an antecolic wide-stoma gastrojejunostomy. These cases will be referred to as the "other operations" group. The operations were performed both by the assigned staff and by the resident surgeons who were in their third and fourth years of training, most operations being done by the latter in both groups of cases. The patient population throughout the period of the study consisted of Army personnel, their dependents, and veterans. Thus the facilities in each group were the same, the surgeons of like training and experience, and the patient population similar.

Materials and Methods

Eighty-five per cent of the patients answered questionnaires which requested information concerning symptoms of the postgastrectomy syn-

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drome. The cases then were categorized into groups with severe, moderately severe, moderate, or mild postgastrectomy syndrome or listed in the group with no evidence of the syndrome. Assignment to the "severe" group indicated that a patient presented a major problem of clinical management. Assignment to the "mild" group indicated that the patient admitted certain symptoms attributable to gastrectomy but had little difficulty. Increasing degrees of severity were noted as moderate and moderately severe.

The incidence and severity of the postgastrectomy syndrome then was correlated with technical components of operation at each follow-up period (1, 3, 6, 12, 24, and 36 months).

A χ^2 method was utilized for determination of significant differences. Comparisons were made between groups of cases, using the number of patients complaining of a symptom and the total number of patients observed. Individual analyses then were performed of each case group pair at each follow-up period by means of four-fold contingency table χ^2 analysis. In all cases in which the expected occurrence within a cell was less than 10, the Yates correction was applied by subtracting 0.5 from the difference between the observed and the expected frequencies.

Results of Gastrectomy for Duodenal Ulcer Disease at Brooke Army Hospital, 1949-1954

Patient satisfaction with operation has been used as a criterion of the efficacy of various surgical procedures. If the majority of patients are satisfied, perhaps the surgeon also should be, but we feel that this subjective factor is a poor estimate of the efficacy of the operative procedure if used alone. When combined with other factors, such as the incidence and severity of sequellae of operation, it becomes of more importance.

Of the 172 patients who indicated satisfaction or dissatisfaction with the result of operation, over 98% (169 patients) stated that they were satisfied, 27% (46 patients) being enthusiastic about the result. Only 6% (11 patients) were only moderately well satisfied. Four patients (2%) expressed dissatisfaction with the result of operation.

Differences in patient reaction account for the degree of satisfaction with an operation almost as much as do the actual results of that operation. Only one of the four patients who were dissatisfied with the operation would be classified from a medical standpoint as a poor result. On the other hand, there have been six cases in which reoperation was necessary. These six patients all expressed satisfaction with operation, albeit somewhat less enthusiastically than others. One of the operations consisted of a bowel resection and lysis of adhesions six months after gastric resection. All the other reoperations were associated with duodenal ulcer disease or with the operation. In one case, which has been reported previously, the patient had severe bronchitis postoperatively and while coughing developed a hernia of the abdominal wall.[2] In addition, the sutures approximating the gastric remnant to the mesocolon apparently gave way, since the patient subsequently developed herniation of the jejunal limbs through the mesocolon and obstruction of the gastroenterostomy on this basis. Since reoperation, he has been symptom-free. One of the patients operated upon for hemorrhage, perforation, and lesser sac abscess subsequently required reoperation for drainage of a recurrent intra-abdominal abscess. Two patients underwent vagotomy for control of recurrent ulcer disease, and one patient underwent re-resection.

The Postgastrectomy Syndrome

The "mild postgastrectomy syndrome" category represents those patients who, when questioned, admit to difficulty but actually are not a clinical problem, while those in the "severe postgastrectomy syndrome" group continue to lose weight despite dietary restrictions and, if the condition does not relent, represent failure of operation. No patient in this series was classified in the "severe" category longer than two years after operation. Although symptoms markedly improved during the first two years, some of the patients (4% of those observed for five years or longer) continued to lose

weight for as long as five years. This incidence probably is misleading since, at two years, only 1% of those observed still were losing weight. These inconsistencies represent a decrease in the number of patients observed at increasing lengths of time after operation rather than an actual increase in the incidence or severity of the syndrome. Failure to regain preoperative weight remained at about 50% of observed cases after the first year, this value approximating that noted in other series.[3-7]

The predominating symptom of the postgastrectomy syndrome was postprandial weakness followed by the need to lie down. Of high incidence also were nausea and abdominal discomfort, these symptoms being essentially equal in frequency. Biliary regurgitation, palpitation, and vomiting were found in a much smaller number of cases and were noted to be of about equal incidence.

Operative Mortality

Nine patients in this entire series died in the postoperative period. They represent a mortality rate of less than 4%. Thirty-two patients were operated upon for control of hemorrhage, and, of these, six died—a mortality rate for these cases of 19%. If all emergency operations for massive hemorrhage are excluded, there remain 213 cases. Three of these patients died—a mortality rate of 1.4% for elective resections.

In three cases death was attributed to leakage of the duodenal stump, and in another this was a contributing factor. In this fourth case, the patient was operated upon because of massive hemorrhage thought to be due to duodenal ulcer. The patient also had known esophageal varices and a duodenal diverticulum, the latter being removed at operation coincident to the gastrectomy. Postoperative hemorrhage, apparently from the esophageal varices, complicated by leakage from the duodenal stump, resulted in the death of the patient. One other patient operated upon for severe hemorrhage also had esophageal varices, and, after resection with control of the bleeding from the duodenal ulcer, the patient died from hemorrhage from the esophageal varices. One patient died following evisceration; another, with pulmonary embolization, and another, with acute pancreatitis following operation. This patient had a history of chronic pancreatitis with a number of acute exacerbations. One patient underwent gastrectomy for acute hemorrhage from a stress ulcer following nephroureterectomy for hydronephrosis and hydroureter. He had postoperative hemorrhage which resulted in his death. The remaining patient who failed to survive operation was moribund on admission, having evidence of perforation of a viscus and mechanical obstruction of the gastric outlet. A feeding jejunostomy was performed, and four days later the patient sustained a massive hemorrhage which required emergency operation. Massive perforation of the distal stomach, pylorus, and proximal duodenum was found at this time. There was a large lesser sac abscess. Resection was performed as a desperate life-saving effort, but the patient failed to recover.

Comparison of the Two Major Case Groups

The two major case groups in this study are the "advocated operation" group (120 cases), the operation being the one presently used at Brooke Army Hospital, and the "other operations" group (125 cases). It is assumed that the follow-up is a true random sampling.

The patient population in the two groups is remarkably constant, the principal differences being in the greater number of dependents and the slightly evener age distribution in the "other operation" group, with a greater number of patients in the 31-40 and the over 60 age groups being found in the "advocated operation" group.

Indications for operation in the two groups differ in that operation apparently was offered with less indication in the "other operation" group than in the "advo-

cated operation" category, since the average duration of the disease was greater in the latter group and here 25% of the operations were performed as emergency operations whereas only 10% of the operations in the "other operation" group were of an emergency nature.

Operation was accomplished for duodenal ulcer in 102 cases in each group, for stomal ulcer in 4 cases and gastric ulcer in 15 cases of the "advocated operation" group, and for stomal ulcer in 4 cases and gastric ulcer in 26 cases in the "other operation" group. Only 22 patients in the entire series were female; the "advocated operation" group includes 7 female patients, and the "other operation" group includes 15 female patients. The ulcer was not removed in 13 cases in the "advocated operation" group, and it was not removed in 9 cases in the "other operation" group.

In the case of operation for massive hemorrhage no great difference could be found between the two case groups with regard to indications for operation; nor could any exact relationship between duration of hemorrhage, age, or severity of hemorrhage and mortality be shown. The only information gained from study of these factors was that the highest mortality, morbidity, and complication rate came from the group who were in the poorest condition at the time of operation.

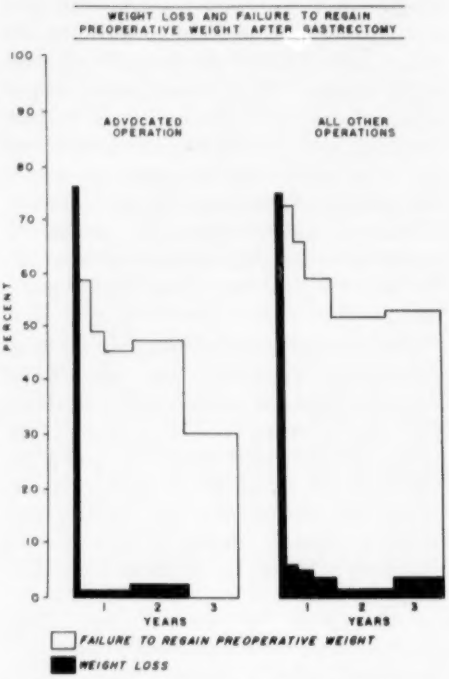


Fig. 2.—The incidence of failure to regain preoperative weight and continuing weight loss following gastrectomy, showing a comparison between the results of the "advocated operation" (120 cases) and "other operations" (125 cases). Results in the first year are indicated at 1, 3, 6, and 12 months after operation.

Fig. 1.—The incidence and severity of the postgastrectomy syndrome, showing a comparison of results in the "advocated operation" (120 cases) group with "other operations" (125 cases). Results in the first year are indicated at 1, 3, 6, and 12 months after operation.

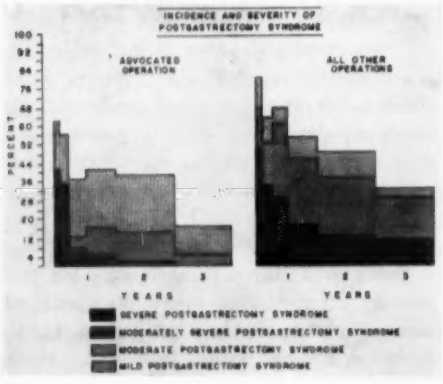


Figure 1 shows the markedly lower incidence of all degrees of the postgastrectomy syndrome in the "advocated operation" group, and in Figure 2 the lower incidence of failure to regain preoperative weight and of weight loss are evident for the "advocated operation" group. The figures taken from the graph are significantly different, many being above the 0.1% level of significance. With the exceptions of the severe postgastrectomy syndrome and/or the incidence of weight loss, where the expected frequency of occurrence is low, almost all the differences are statistically significant. In those cases in which the expected frequency of occurrence is below 10 in any cell, the Yates correction has been applied. This

results in overcorrection but is thought to be necessary to prevent invalid assumptions based on insignificant findings. These findings indicate that there is a significantly lower incidence and reduced severity of the postgastrectomy syndrome when the "advocated operation" is used.

Effect of the Extent of Gastric Resection

At Brooke Army Hospital, as at most other hospitals, the extent of resection has been estimated by the surgeon. This method is inexact, but, without question, a surgeon who plans to remove 75% of the stomach will remove more of the organ than will the surgeon who plans to remove 50% or 60% of the stomach. Various methods of measurement have been devised. Wangensteen [8] used measurement of the mucosa removed at operation as a criterion for determination of adequacy of operation, as he felt that the fundus was the most dilatable portion of the stomach. Finsterer and Cunha, however, found that the fundus does not dilate appreciably while still in continuity with the remainder of the stomach and dilates only after gastrectomy has removed the distal stomach. Visick,[9,10] considering any measurement of removed tissue useless in the estimation of the adequacy of gastrectomy, measured the stomach remnant at operation. His conclusions after 505 "measured gastrectomies" was that an adequate gastrectomy was accomplished when the line of transection passed above the lowest of the short gastric vessels. This he estimated to be a "75%" gastric resection.

Regardless of the method used for estimation of the extent of resection, it is generally agreed that, to be effective in the treatment of duodenal ulcer disease, gastrectomy must be rather radical.

In this series, there was an increased frequency of the postgastrectomy syndrome associated with those operations in which less than 75% of the stomach was removed, although the severity of the syndrome appeared to be more pronounced when a greater amount of stomach was resected. These differences do not appear to be statistically significant. The values for χ^2 in no instance are greater than 2.71, the critical value for χ^2 at one degree of freedom and at the 10% level of significance.

The influence of the extent of resection on postoperative weight also is inconclusive. At one month there is a statistically significant difference in that a smaller number of patients report weight loss the month after operation when the smaller resection is done. After the first month, however, there is not a significant difference either in continued weight loss or in failure to regain preoperative weight.

Further evaluation of the effect of the extent of resection with regard to the postgastrectomy syndrome is impossible without consideration of the associated technical features of the operations and the interactions resulting therefrom. The literature indicates that the small stoma is a major factor in the reduction of the incidence and severity of the postgastrectomy syndrome. The small stoma was used in 78% of the cases in which the smaller resection was performed. The short retrocolic afferent loop also has been suggested as a factor in reduction of the incidence of the syndrome, and it was used in 75% of the group in which the greater resection was done and in only 23% of the other group. The antiperistaltic anastomosis is preferred, since it allows a shorter afferent loop and is not apt to become kinked. This may play some part also in the reduction of the incidence and severity of the postgastrectomy syndrome, and, again, the frequent association of the greater resection and the factor thought to be apt to reduce the incidence of the syndrome is noted, while the group in which the isoperistaltic anastomosis is found in greatest frequency is that in which the smaller resection was performed.

Despite the increased frequency of association of techniques which are thought to decrease the incidence of the postgastrectomy syndrome with the greater

extent of resection, there is little evidence here of improved results with regard to the postgastrectomy syndrome following the more extensive resection. Increased extent of resection must result in increase in the incidence and severity of the postgastrectomy syndrome only if the small stoma, the retrocolic anastomosis, and the antiperistaltic anastomosis can be shown to be superior to other techniques.

Comparison of all cases in which retrocolic antiperistaltic small-stoma anastomoses were used with all other operations performed reveals a considerably lower incidence and less severity of the postgastrectomy syndrome in the former. Figures 3 and 4 show this comparison, which appears from the values of χ^2 to represent a significant difference. This, we feel, establishes the fact that the incidence and severity of the postgastrectomy syndrome are directly proportional to the extent of gastric resection.

Effect of the Length of the Afferent Loop

The length of the afferent loop is determined, principally, by the relationship of the anastomosis to the colon. While advocates of antecolic anastomoses sometimes claim that this type anastomosis is made with a short afferent loop, it is obvious that the afferent loop can be made shorter if a retrocolic anastomosis is used. The relationship of the length of the afferent jejunal loop to the postgastrectomy syndrome, therefore, will be studied by comparison of the results following retrocolic anastomoses as compared with antecolic anastomoses.

There appears to be a lower incidence and less severity of the postgastrectomy syndrome following the retrocolic anastomosis, particularly with regard to the more severe classifications of the syndrome, as is shown in Figure 5. Preoperative weight was regained in a higher proportion of the patients and weight loss continued in a lower proportion of the patients who had retrocolic

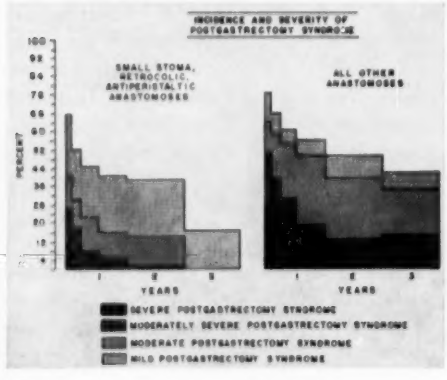


Fig. 3.—Incidence and severity of the postgastrectomy syndrome. The effect of retrocolic antiperistaltic small-stoma anastomosis (128 cases) versus other types of anastomoses (117 cases). The importance of these factors contributes to the indication that the postgastrectomy syndrome more frequently follows radical resection. Results in the first year are indicated at 1, 3, 6, and 12 months after operation.

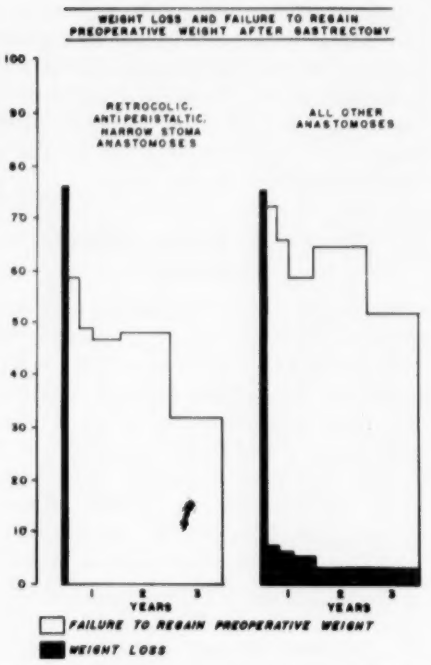


Fig. 4.—Incidence of weight loss and failure to regain preoperative weight. The effect of retrocolic antiperistaltic small-stoma anastomosis. The importance of these factors contributes to the indication that the postgastrectomy syndrome is adversely affected by radical gastric resection. Results in the first year are indicated at 1, 3, 6, and 12 months after operation.

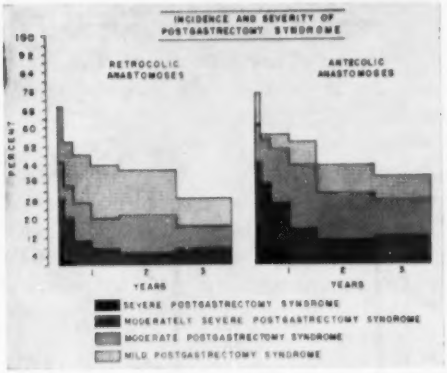


Fig. 5.—The incidence and severity of the postgastrectomy syndrome. The effect of the length of the afferent jejunal loop. Retrocolic anastomosis (142 cases) versus antecolic anastomosis (103 cases). Results in the first year are indicated at 1, 3, 6, and 12 months after operation.

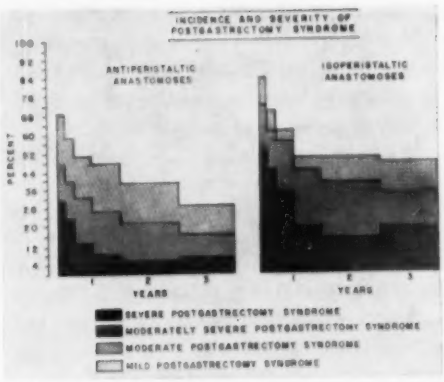


Fig. 7.—The incidence and severity of the postgastrectomy syndrome. The effect of the peristaltic relationship of the gastrojejunostomy. Antiperistaltic anastomoses (196 cases) versus isoperistaltic anastomosis (49 cases). The results in the first year are indicated at 1, 3, 6, and 12 months after operation.

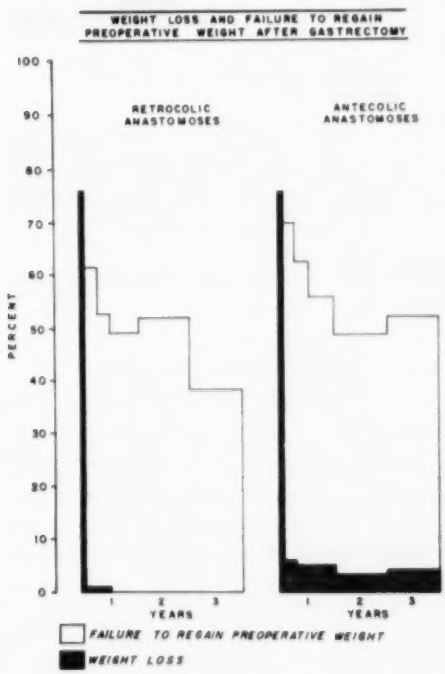


Fig. 6.—The incidence of weight loss and failure to regain preoperative weight. The effect of the length of the afferent loop. Retrocolic anastomosis (142 cases) versus antecolic anastomosis (103 cases). Results in the first year are indicated at 1, 3, 6, and 12 months after operation.

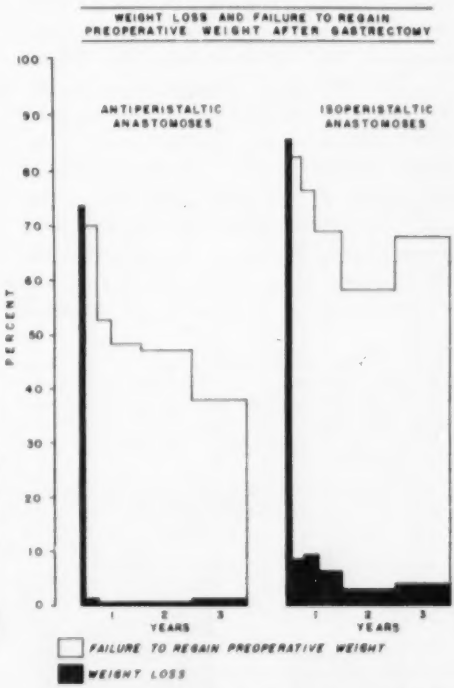


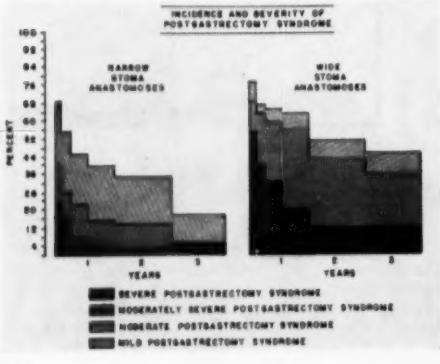
Fig. 8.—The incidence of weight loss and failure to regain preoperative weight after gastrectomy. The effect of the peristaltic relationship of the gastrojejunostomy. Antiperistaltic anastomoses (196 cases) versus isoperistaltic anastomoses (49 cases). The results in the first year are indicated at 1, 3, 6, and 12 months after operation.

anastomoses. This is shown in Figure 6. Approximately one-third of the figures appeared to be significantly different as evidenced by the tabulation of the values of χ^2. Inasmuch as most of the retrocolic anastomoses were associated with 75% or greater resection and narrow-stoma antiperistaltic anastomoses, while the antecolic anastomoses were associated with a higher proportion of operations in which less resection was done with isoperistaltic anastomoses and wide stomas, it must be assumed that the retrocolic anastomosis plays at least a minor role in the reduction of the incidence and severity of the postgastrectomy syndrome.

Effect of the Peristaltic Relationship of the Gastrojejunostomy

Figure 7 shows a smaller degree of the postgastrectomy syndrome following operation in which an antiperistaltic anastomosis was used, and Figure 8 shows that difficulties with regard to maintenance of weight also are less frequently encountered here than with the isoperistaltic anastomoses. Approximately one-third of these differences are found to be statistically significant. Since the associated technical factors tend to cancel out, it may be assumed that the antiperistaltic anastomosis also plays a minor role in the reduction of the incidence and severity of the postgastrectomy syndrome.

Fig. 9.—The incidence and severity of the postgastrectomy syndrome. The effect of size of the gastrojejunostomy stoma. Small stoma (150 cases) versus wide stoma (95 cases). The results in the first year are indicated at 1, 3, 6, and 12 months after operation.



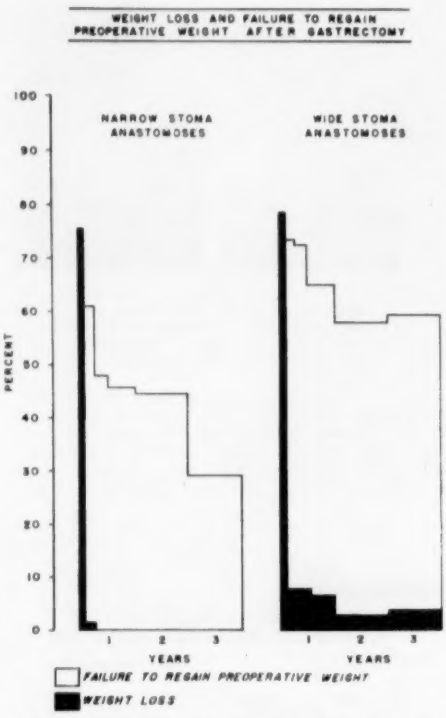


Fig. 10.—The incidence of weight loss and failure to regain preoperative weight. The effect of the size of the gastrojejunostomy stoma. Small stoma (150 cases) versus wide stoma (95 cases). The results in the first year are indicated at 1, 3, 6, and 12 months after operation.

Effect of the Size of the Gastrojejunostomy Stoma

There was a marked difference in the incidence and severity of the postgastrectomy syndrome associated with variation in the size of the gastroenterostomy stoma. In Figure 9 it can be seen that the duration of all degrees of severity of the syndrome is less after operation in which the narrow stoma is utilized. The advantage of the small stoma is even more obvious in Figure 10, where the incidence of continued weight loss and failure to regain preoperative weight have been indicated. These differences are statistically significant. Since most

of the operations in which the narrow stoma was used entailed greater than 75% resection and the operations in which the wide stoma was used were those in which the majority were smaller resections, the narrow stoma must be held primarily responsible for the reduced incidence and lessened severity of the postgastrectomy syndrome—the retrocolic anastomosis, the antiperistaltic anastomosis, and the lesser resection playing more minor roles in this effect.

midway of the chart, this should indicate that considerably less importance can be attributed to the relation of the anastomosis to peristalsis than to the size of the stoma. All other factors appear to be of minor importance.

Figure 12 ranks the technical factors according to the frequency and duration of the complaint of failure to regain preoperative weight, and here the size of the stoma and the relation of the anastomosis to peristalsis

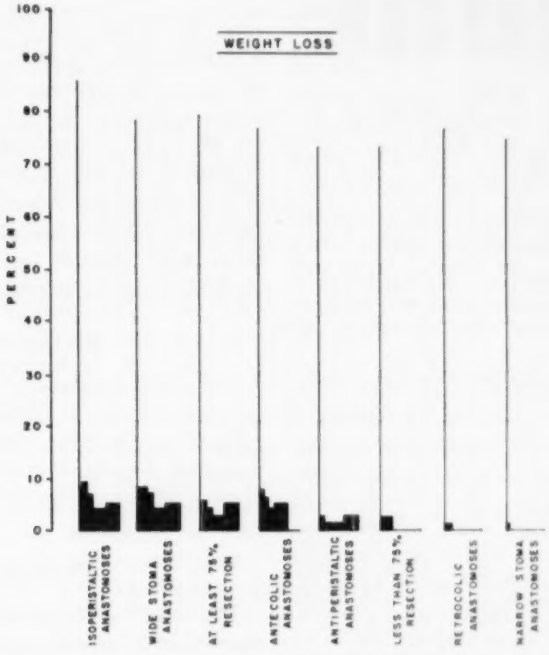


Fig. 11.—The incidence and duration of weight loss and its association with various techniques of gastrectomy. In the horizontal axis of each of these graph forms, follow-up results at 1, 3, 6, 12, 24, and 36 months are indicated by a distance proportionate to the elapsed time.

Maintenance of Weight

It can be seen in Figure 11 that the size of the stoma is the most important factor in the determination of the incidence and duration of continued weight loss, although the isoperistaltic anastomosis group is ranked first on the chart. Since the antiperistaltic anastomosis group is ranked almost

appear to occupy positions of relatively equal importance. From consideration of Figures 1 and 2, it would appear to be a logical assumption that the most important factor in the reduction of the incidence difficulty with regard to weight maintenance would be the small stoma and of secondary importance would be the antiperistaltic anastomosis.

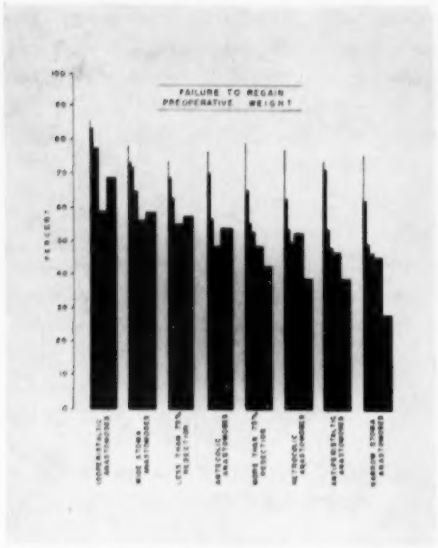


Fig. 12.—The incidence and duration of failure to regain preoperative weight following gastrectomy. This chart shows the association of various technical factors with this symptom. In the horizontal axis of each of these graph forms, follow-up results at 1, 3, 6, 12, 24, and 36 months are indicated by a distance proportionate to the elapsed time.

Weakness and The Need to Lie Down

The size of the stoma and the relation of the anastomosis to the colon affect the incidence and duration of the symptom, weakness, almost equally. From this it would appear that the narrow stoma and the retrocolic anastomosis are equally important in the prevention of weakness following meals. The need to lie down is associated with this symptom, and the narrow stoma also is of prime importance in prevention of the need to lie down, the retrocolic anastomosis being of some lesser importance in this regard.

Nausea

While the isoperistaltic anastomosis is most frequently associated with nausea, an equally significant effect is noted in relation to the size of the stoma, the narrow stoma again being the least offending factor.

Abdominal Discomfort

Abdominal discomfort after meals also was noted most frequently following isoperistaltic anastomoses, and here the narrow stoma and the antiperistaltic anastomosis appear to be equally efficacious in reduction of this symptom.

Biliary Regurgitation

Biliary regurgitation has been suggested by some authors as not part of the "dumping syndrome" but as due to the extent of resection or some other factor which was not responsible for production of most of the postgastrectomy syndrome. We find no evidence of the importance of the extent of resection in the production of the symptom and, further, no evidence of importance of the narrow stoma. This would lend support to the belief that the major portion of the postgastrectomy syndrome is due to factors other than those causing biliary regurgitation. Apparently factors which increase the incidence of this symptom are the antiperistaltic and retrocolic anastomoses, which seem to be equally important.

Palpitation

Palpitation apparently is less common in association with the narrow stoma and the retrocolic anastomosis. Other factors are of secondary importance, although the least important appears to be the extent of resection.

Vomiting

The technical factor most frequently associated with vomiting seems to be the wide stoma. Since the narrow stoma is the least frequent offender, this relationship appears to be significant. The other factors appear not to be of importance.

Constipation and Diarrhea

Although constipation was considered not part of the postgastrectomy syndrome and the symptom was included in the questionnaire only to aid in the evaluation of the answers with regard to diarrhea, there appears to be a relationship between the technical factors of operation and the symptom.

Here the isoperistaltic and antecolic anastomoses appear to result in the lowest incidence of constipation. The narrow stoma and, of secondary importance, the antiperistaltic anastomosis appear to result in reduced incidence of diarrhea. It is interesting to note that a comparison of these two symptoms reveals a more definite association between the techniques of operation and constipation than between these technical factors and the incidence of diarrhea.

Comment

Analysis of the effect of various technical components of operation on the incidence and duration of specific symptoms of the postgastrectomy syndrome reveals that the narrow stoma is of primary importance in prevention of the need to lie down after meals, weight loss, postprandial vomiting, and diarrhea, the narrow stoma being a major factor in prevention of the symptoms of failure to regain preoperative weight, postprandial weakness, nausea, abdominal discomfort, and palpitation. In short, the narrow stoma appears to be the most important factor in the reduction of the individual symptoms of the postgastrectomy syndrome.

The retrocolic anastomosis appears to be of importance in the prevention of postprandial weakness, palpitation, and the need to lie down. An antiperistaltic anastomosis would seem to reduce the incidence of failure to regain preoperative weight, nausea, abdominal discomfort, and diarrhea.

Constipation and biliary regurgitation appear to be associated with antiperistaltic and retrocolic anastomoses. These probably are the least important of the symptoms associated with gastrectomy, and the increased incidence can be accepted since the advantages of decreased incidence of the other symptoms associated with the postgastrectomy syndrome makes the retrocolic antiperistaltic anastomosis the most satisfactory type.

The tenet held by some that biliary regurgitation is not a part of the "dumping syndrome" and that it is caused by factors other than those causing the "dumping syndrome" is supported by this study. The postgastrectomy syndrome appears to be the result of a number of factors, and in all probability psychogenic, dietary, and perhaps other sources may be incriminated. The technical components of operation, however, are prime factors in the production or prevention of the postgastrectomy syndrome. From this study there would appear to be four distinct mechanisms in the production of this syndrome. They are jejunal distention brought about by rapid gastric evacuation, traction on the gastric remnant and the afferent loop, partial obstruction of the stoma by kinking of the jejunum at the anastomosis, and reflux of afferent loop contents into the gastric remnant.

Rapid gastric evacuation and jejunal distention result from the use of too wide a gastrojejunostomy stoma and by sympathetic stimulation produce nausea and vomiting, palpitation and the need to lie down, hyperperistalsis, diarrhea, and postprandial abdominal discomfort. Correction of this fault of gastrectomy consists simply of the construction of a small gastrojejunostomy stoma. It need be no larger than the jejunum into which it empties.

Traction on the afferent loop and the gastric remnant, through sympathetic stimulation, may produce the same symptoms. Distribution of the weight of the gastric remnant and the afferent loop over a large area may be accomplished by the use of the retrocolic anastomosis, securing the gastric remnant throughout its width to the small bowel and to the transverse mesocolon. The weight of the afferent loop may be reduced by shortening it. The no-loop gastrojejunostomy is the ultimate in this respect, since the lesser curvature aspect of the gastric remnant is sutured to distal duodenum.

Partial obstruction of the stoma may be produced by an isoperistaltic retrocolic anastomosis or by an antecolic anastomosis, resulting in nausea, vomiting, and abdominal discomfort. This is readily corrected by the

use of the more nearly anatomically correct antiperistaltic anastomosis.

Reflux of afferent loop contents into the gastric remnant results in biliary regurgitation and constipation. This is more common following the retrocolic antiperistaltic anastomosis, but it is acceptable in view of the many advantages of this type of anastomosis.

The operation which combines the factors shown to be of most importance in the prevention of symptoms of the postgastrectomy syndrome with those factors considered important in the prevention of recurrent duodenal ulcer disease consists of resection of at least 75% of the stomach with all the antral mucosa and reconstruction of gastrointestinal continuity by means of a retrocolic no-loop antiperistaltic small-stoma gastrojejunostomy.

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Unusual Complications of Subtotal Gastric Resection

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Subtotal resection of the stomach was performed first in man by Jules Pean in 1879 for treatment of a gastric carcinoma. Subsequently, in 1915, von Hoberer was the first to perform and recommend gastric resection for treatment of recalcitrant peptic ulcers. During the four decades since this procedure was first recommended as treatment for a benign disease, it has been utilized for the management of an array of pathological entities involving the esophagus, stomach, and duodenum.

The morbidity and mortality rates associated with subtotal gastric resection vary with the indications for operation, the physical condition of the patients, and the type of resections employed. Although an understanding of these and other factors has contributed to a lowered morbidity, further reduction in the number of complications will result by continuing to emphasize their occurrence. Five complications of subtotal gastrectomy are reported in this paper which are unusual in our experience; however, they are not such curiosities that their reporting will be of little practical value. On the contrary, since each complication involves important surgical principles, it is our opinion that additional emphasis should be given to them as potential hazards of gastric surgery.

Report of Cases

Complications of Excessive Mobilization of the Stomach

CASE 1.—A 61-year-old white man entered the hospital because of hematemesis and melena. At the time of admission, the patient was in a state of peripheral vascular collapse; his hemoglobin was 3.9 gm. per 100 cc. Although the patient responded temporarily to aggressive medical ulcer therapy, including blood transfusions, the recurrence of bleeding necessitated an emergency operation.

A bleeding ulcer, situated high on the lesser curvature approximately 4 cm. from the esophagogastric junction, was found. A subtotal gastric resection that included the ulcer in the specimen was performed; gastrointestinal continuity was easily restored by a Billroth I anastomosis.

The postoperative course was slow but uncomplicated until the eighth day, at which time a fluctuant mass in the left epigastrium and signs of peritonitis suggested the diagnosis of small bowel obstruction with compromise of its blood supply. At exploration, necrosis of the remaining gastric pouch and a large left subphrenic abscess were found. After the necrotic stomach was removed, a Roux-en-Y esophagojejunostomy and drainage of the duodenal stump with a mushroom catheter were performed. One hour postoperatively, the patient died.

CASE 2.—A 72-year-old white man was admitted to the hospital because of diarrhea, vomiting, and weakness of two days' duration and a past history suggestive of peptic ulcer. On admission, the hemoglobin was 4.8 gm. per 100 cc.; roentgenograms of the upper gastrointestinal tract revealed a large gastric ulcer within a hiatus hernia. Although the patient improved with transfusions and a vigorous ulcer regimen, bleeding continued at a slow but steady rate. Operation was initially deferred because of severe heart disease, but on the 27th hospital day a massive hemorrhage occurred which necessitated an emergency operation.

A large ulcer on the lesser curvature of the stomach near the esophagogastric junction was removed by high subtotal gastric resection, and continuity of the gastrointestinal tract was reestablished by an anticolic isoperistaltic gastrojejunostomy. The hiatal hernia was also repaired.

On the sixth postoperative day, the patient was reoperated upon because of generalized peritonitis. At exploration, the gastric remnant and the two limbs of the gastrojejunostomy were found to have rotated nearly 180 degrees in a counterclockwise direction. The gastric pouch was viable, but leakage had occurred at the suture line. The

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volvulus was reduced; the suture lines were reinforced, and the gastric pouch was secured to prevent recurrence of volvulus. The patient died 36 hours after operation.

Comments on Cases 1 and 2.—These two cases emphasize the fact that excessive mobilization and devascularization of the stomach at the time of gastric resection are sometimes accompanied by serious consequences. Excessive freeing of the greater and lesser curvatures of the stomach permitted the development of gangrene of the gastric pouch in Case 1 and volvulus of the gastric pouch in Case 2. In the latter case, preservation of the last two or three vasa brevia did not provide adequate stabilization to prevent the occurrence of volvulus of the gastric pouch, whereas a retrocolic, rather than the antecolic, gastrojejunostomy might have prevented this complication. Organaxial volvulus of the stomach is frequently associated with a hiatus hernia. In this case it appears that the additional mobilization required for hernia repair rather than the existence of the hernia may have contributed to the complication of volvulus.

Complications Resulting from Disposition Made of the Gastrocolic Ligament

Case 3.—A 72-year-old white man with symptoms of a duodenal ulcer for 20 years and three known episodes of gastrointestinal bleeding was advised to have an operation because his ulcer pain was refractory to medical management. A 60% subtotal gastric resection and an anticolic Billroth II anastomosis were performed.

On the fifth postoperative day physical findings suggested the diagnosis of a left subdiaphragmatic abscess, which, at operation, was found to be associated with infarction of the greater omentum. Following excision of the omentum and drainage of the abscess, an uncomplicated postoperative course ensued.

Case 4.—A 64-year-old white man was admitted to the hospital because of abdominal pain and vomiting. Six months previously an emergency subtotal gastric resection and an omentectomy had been performed following perforation of a gastric ulcer at gastroscopy. Pathologic study of the stomach at that time revealed the presence of adenocarcinoma.

On the second admission physical examination revealed no signs of peritonitis but the abdomen was tender and the bowel sounds were hypoactive. An emergency barium enema revealed a free flow of barium to the hepatic flexure, where its progress was completely obstructed. After this procedure, signs of peritoneal irritation developed, but repeat roentgenographic examination revealed no air or barium within the peritoneal cavity.

At operation, no carcinoma was discernible; instead, volvulus of the redundant transverse colon was found. The colon was viable and easily reduced, following which the hepatic flexure was suspended to prevent recurrence. The patient died 12 hours postoperatively of pulmonary edema.

Comments on Cases 3 and 4.—The complication of omental necrosis in Case 3 is a reminder that one can not be indiscriminate with the blood supply of the greater omentum and that the gastrocolic ligament, if it is retained, should be separated from the stomach within the vascular arcade in order to insure its adequate blood supply.

The factors responsible for initiating volvulus of the transverse colon in Case 4, six months after omentectomy, are not clear. In the absence of any anomalies of rotation, however, it would appear that the redundant transverse colon on a long mesocolon was unable to maintain its normal anatomical position after the support contributed by the gastrocolic omentum was removed. The complication of transverse colon volvulus suggests that omentectomy should carefully be considered before it is routinely applied during gastric resection for benign disease. If the colon appears abnormally redundant, attempts to anchor the flexures should be made.

Complication Resulting from Injury of the Pancreaticobiliary Ducts

Case 5.—A 37-year-old white man with a 16-year history of duodenal ulcer was admitted to the hospital because of recent hematemesis and melena. Six years prior to admission a posterior gastroenterostomy had been performed for duodenal ulcer. Subsequently, a gastrojejunocolic fistula developed which required four operations; none of them was treatment for the peptic ulcer. Clinical evaluation and laboratory studies of the patient at the time of admission indicated the necessity for definitive ulcer therapy.

At operation, a 75% subtotal gastrectomy and a Billroth II anastomosis were performed for an

active ulcer on the posterior wall of the badly deformed duodenum. On the first postoperative day the patient developed signs of peritoneal irritation and an elevated serum amylase was noted. On the third postoperative day he was reexplored because of jaundice and signs of peritonitis. Fluid in the abdominal cavity, an inflammatory process in the region of the head of the pancreas, and failure of the distended gallbladder to empty on compression suggested the diagnosis of acute pancreatitis. Cholecystostomy and drainage of the abdomen were performed. After this procedure the patient's condition improved, until an episode of intra-abdominal bleeding occurred. He was subsequently explored three times for hemorrhage, without any definite bleeding point being found. On the 48th day after the first operation the patient died.

Postmortem examination revealed that the closure of the duodenal stump had encroached upon the ampulla of Vater. In addition, the common duct and the main pancreatic duct were no longer in continuity with the duodenum; instead, bile and pancreatic juice were able to pass freely into the peritoneal cavity. Fat necrosis was found within the abdomen; the pancreas, however, appeared normal on gross inspection of the cut section and on microscopic examination.

Comments on Case 5.—The inflammation associated with the ulcer in this patient resulted in a shortening of the duodenum. As a result of this anatomical alteration, closure of the duodenal stump occluded the ampulla of Vater, obstructing the common bile duct and the pancreatic duct of Wirsung. If the ampulla was obstructed in this manner, it is not unreasonable to postulate that the duct of Santorini was transected during the mobilization of the duodenum. Transection of this duct without ligation would explain the immediate postoperative peritonitis and the high amylase content of the peritoneal fluid at the time that the ampulla of Vater appeared obstructed. The peritoneal inflammatory reaction and pressure necrosis produced by closure of the duodenum may have resulted in the eventual dissolution of the continuity of the common duct and the duct of Wirsung. The drainage of these two ducts into the peritoneal cavity undoubtedly resulted in the extensive necrosis and hemorrhage that finally caused the patient's death.

General Comment

Excessive Mobilization of the Stomach.—The surgical management of gastric ulcers located in the cardia has been a subject of considerable discussion. Cases 1 and 2 serve as reminders that the overenthusiastic mobilization required to resect ulcers in this location cannot always be performed without danger.

The rich anastomotic vascular supply of the stomach has been described in many textbooks, and the impression is gained from these sources that the arterial supply of the stomach can be sacrificed as far as necessary to allow adequate mobilization for resection. Experimental work in dogs, however, has indicated that there are well-defined limits of devascularization which the stomach is able to tolerate. Bernheim [1] showed that either the lesser or the greater curvature could be totally devascularized without ill effects, as could the whole of one curvature and part of the other, but that if all vessels were ligated gangrene developed along the greater curvature.

References to the possibility of such occurrences in man following gastric resection have been meager. Smith [14] stated that high resections may be associated with gastric perforation as a result of impairment of the stomach's blood supply. During the past two decades, the only case report of necrosis of the gastric pouch following excessive mobilization of the stomach was made by Rutter in 1953.[13] This patient was 40 years of age (considerably younger than our patient) and had an ulcer located high in the cardia. The only other case of a similar nature with which we are familiar was described by Arthur Gore.[4] His patient was a 54-year-old man in whom necrosis of the gastric remnant also occurred following the excessive mobilization required to resect a gastric ulcer that lay high in the cardia.

There is probably little danger of ischemic necrosis of the gastric pouch associated with a routine subtotal gastrectomy; however, this is a real danger in elderly patients with generalized arteriosclerosis when

high resections for juxtaesophageal gastric ulcers are performed. To avoid such an irreparable disaster, the blood supply to the greater curvature should be carefully considered, and at least the uppermost vasa brevia should be jealously safeguarded, even at the expense of free mobilization.

Volvulus of the intact stomach is a rare occurrence but has been reported numerous times. On the other hand, volvulus of the gastric remnant following subtotal gastric resection has rarely been described.[12] Volvulus after gastrectomy is most likely to occur if the greater and lesser curvatures are mobilized to the esophagogastric junction and a long-loop, anticolic gastrojejunostomy is performed. Angulation that may be produced by a gastrojejunostomy which extends from the mesenteric border of the jejunum to the antimesenteric border will also predispose to volvulus.

Juxtaesophageal gastric ulcers have provided a difficult surgical problem because of the technical difficulties and the nutritional defects imposed by high subtotal gastric resections. The evidence presented by Dragstedt[2] which suggests that gastric ulcers are primarily due to the hyperactivity of the antral gastrin mechanism has provided a physiological basis for the treatment of gastric ulcers by wedge resection of the ulcer for biopsy and antrectomy if the ulcer is benign. Our complications with high subtotal gastrectomies provide additional reasons for treatment of a benign ulcer near the esophagus with a conservative distal resection, if conditions in the individual case warrant.

Disposition of the Gastrocolic Omentum

In the majority of gastric resections for peptic ulcer, it appears to be unimportant what disposition is made of the gastrocolic omentum; however, complications that are directly related to this aspect of the operation do occur. Following gastrectomy, Fritzsche[3] observed two patients in whom necrosis of the greater omentum contributed to their deaths. The necrosis was attributed to the ligation of both gastroepiploic arteries while the omentum was left in situ. As a result of subsequent anatomical injection studies, he recommended the preservation of the omental circulation by ligating the gastrocolic ligament close to the gastric wall inside of the gastroepiploic arcade.

Horton[5] studied the anastomoses between the branches of the right and left gastroepiploic arteries and made particular reference to a large branch of the left gastroepiploic artery which ran caudalward and to the right in the anterior omental leaf. He stated that this "oblique artery" was constantly present and accounted for the great rarity of omental necrosis after an operation which had apparently destroyed nearly all of its blood supply. Although this vessel may be present constantly, it is undoubtedly subject to natural variations in position, course, and caliber, which cause its effectiveness in the prevention of necrosis to be unpredictable.

Recently, Kirschner and Garlock[6] reported the morbidity of two groups of gastrectomized patients. In the first group, operated upon for carcinoma of the stomach, the omentum was removed; in the second group, operated upon for duodenal ulcer, it was not removed. In the latter group, these authors attributed an increased morbidity to small areas of necrosis of the gastrocolic omentum. Because of this experience, as well as their experimental studies on the blood supply of the dog's omentum, they recommend the routine removal of the gastrocolic ligament.

We have found no previous reference to volvulus of the transverse colon occurring as a complication of omentectomy and gastric resection, except the report by Zwicker of volvulus of the transverse colon that appeared to be associated with an anomaly of the mesocolon.[16] Volvulus of the transverse colon following omentectomy is undoubtedly a rare complication; the fact that it can occur, however, indicates that this eventuality must be considered when routine

omentectomy is undertaken during gastric resection.

Removal of the gastrocolic ligament during subtotal gastrectomy for benign diseases is probably an individual matter. It is best applied in the obese person, where removal of the omentum is most likely to facilitate surgery and minimize the danger of fat necrosis. If the gastrocolic ligament is removed, the transverse colon, when redundant, should be stabilized by appropriate sutures. If the gastrocolic ligament is to remain in situ, the lowest morbidity will be maintained by detaching the ligament from the stomach within the gastroepiploic arcade.

Injury of the Pancreaticobiliary Ducts.—Scarring that results from a posterior penetrating duodenal ulcer can shorten the duodenum and hepatoduodenal ligament and cause distortion of the common bile duct. Gastrectomy performed for an ulcer of this type may be complicated by injury to the pancreatic ducts, the common bile duct, or the ampulla of Vater.

The onset of jaundice after gastric resection, if not the result of hepatocellular damage, may be the result of traumatic or inflammatory obstruction of the extrahepatic biliary tree. Jaundice due to traumatic obstruction may be either direct, from transection of the common duct or obstruction of the ampulla of Vater by the duodenal stump closure, or indirect, by angulation, torsion, and eventually stricture formation of the common duct.

Kourais [7] and Perazzo [11] have described the occurrence of jaundice after gastric resection and emphasized the fact that an inflammatory reaction associated with operation for posterior penetrating ulcer may be sufficient to obstruct the common bile duct. Obstruction of the pancreatic duct in a similar manner has also been reported as the cause of pancreatitis and pancreatic cysts. Nicolo [10] reported four cases of jaundice which resulted from obstruction of the intrapancreatic portion of the common duct by pancreatic fibrosis. The obstructive jaundice in these cases appeared to be the result of localized pancreatitis aggravated by extensive surgery required to resect a posterior penetrating duodenal ulcer.

Although it is recognized that gastric resection may be associated with injury to the common duct and the duct of Wirsung, the possibility and significance of injury to the duct of Santorini has not been sufficiently appreciated. Millbourn [9] and Warren [15] have pointed out that the duct of Santorini, being more superficial and entering the duodenum proximal to the ampulla of Vater, is more vulnerable during mobilization of a large or low-lying posterior duodenal ulcer than is the duct of Wirsung. In cases of this type, the duct of Santorini may inadvertently be transected and either ligated or left to drain into the peritoneal cavity. The consequences of this depend upon the functional importance of the duct. If the duct of Santorini has carried the major, or even a large, proportion of the external pancreatic secretions to the duodenum, as is the case in 10% to 20% of patients, the results of its injury may well be serious, if not disastrous. Indeed, such injury may be the explanation for some cases of postoperative pancreatitis where the duodenum was adherent to the head of the pancreas but was mobilized "without undue trauma to the pancreas."

The dangers of injury to the common bile duct and pancreatic ducts at the time of gastrectomy for an acute low-lying posterior ulcer are sufficiently great to warrant a conservative ulcer operation, such as vagotomy and an ancillary drainage procedure. If gastric resection is deemed necessary, however, the number of injuries to the common bile duct and the duct of Wirsung will be reduced if the course of the common duct is identified by a long-arm T-tube placed within it lumen, as advised by Lahey.[8]

Summary and Conclusions

Excessive mobilization of the greater and lesser curvatures of the stomach can result

in necrosis or volvulus of the gastric remnant. These complications provide additional justification for the management of benign juxtaesophageal gastric ulcers by distal subtotal gastric resection.

The disposition of the gastrocolic omentum during subtotal gastric resection for benign diseases is an individual problem. If the omentum is not removed, it should be detached from the stomach within the gastroepiploic arcade to preserve its blood supply. Removal of the omentum may be associated with volvulus of the transverse colon if the latter is redundant or has a long mesentery.

Obstructive jaundice and acute pancreatitis can result from injury of the common bile duct or pancreatic ducts when subtotal gastric resection is performed for an acute posterior penetrating duodenal ulcer. The duct of Santorini may be more vulnerable than the duct of Wirsung, and the consequences of its injury may be equally as serious.

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Surgery Illustrated

Right Hemicolectomy

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This article, and three that will follow in subsequent issues of the ARCHIVES, are based on an Atlas [1] that was prepared primarily for the surgical trainee—the surgical intern, the assistant resident, the resident, and the fellow in surgery—in the belief that a sufficiently detailed atlas will prove to be of great aid to the reader in either assisting at or performing a particular operation. Each operation is profusely illustrated in detail to give the step-by-step technique, thus making the operative procedure entirely clear.

The operative techniques that are illustrated are those that have proved most satisfactory to the author, and each operation is discussed by a surgeon with great experience in the performance of that particular operation. Each discussant was asked to stress any points of disagreement with the author and to illustrate whatever steps or variations in the operative technique that have proved most satisfactory to him.

An outstanding feature of the Atlas and these exhibits is the fact that Alfred Feinberg, the medical artist, was present at the operation table when he sketched, sometimes three or four times, each of the operations that he has illustrated. Thus, anatomic realism, as well as the creative interpretation of the artist, was realized. The reader sees a true portrayal of the anatomy of the region and step-by-step technique of the operation.

Comment

Right Radical Hemicolectomy

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It is in the right side of the colon that one finds many of the "bulky" neoplasms, which experience has shown to have a far better prognosis than some of the smaller types. A radical attack is often rewarded by cure, even when the abdominal wall or adjacent viscera are invaded.

Dr. Madden has outlined, compactly but thoroughly, the steps in the rather well-standardized modern "right hemicolectomy," and he leaves little for the discusser to contribute by way of alteration or addition. It might be well to remind the surgeon that thorough exploration (by palpation) of the entire abdomen should *precede* local inspection of the colonic lesion, lest he become so fascinated with the excision as to forget the exploration entirely. Then, too, an abscess may be encountered alongside the lesion when least expected, which may make it unwise to proceed with exploration of the rest of the abdominal cavity.

Exposure should be adequate and reasonably quick. I prefer an incision slightly more lateral than that shown in Plate 1*A*, with division of the rectus in

1. Madden, J. L.: Atlas of Technics in Surgery, New York, Appleton-Century-Crofts, Inc., to be published September, 1957.

Department of Surgery, St. Clare's Hospital, 415 W. 51st St. (19).

the same line rather than retraction of the muscle outward. Retraction is tedious and limits exposure to some degree. An oblique right lower abdominal incision is an excellent alternate choice, as it affords enough exposure and is the "strongest" subsequently.

If a cecal cancer is encountered unexpectedly during surgery for appendicitis (through a McBurney incision), access for a right hemicolectomy can be gained by extending the small incision medially and dividing the rectus sheath. The hepatic flexure is very rarely at as high a level as indicated in Plate I*D*, *E*, and *F*; and on several occasions, I have easily removed the right colon through such an incision.

The division of the lateral peritoneum, as in *D*, might well be at a site farther removed from the growth. If the neoplasms is adherent to the lateral wall, a row of Kocher clamps on the peritoneum and posterior sheath, rather than retractors, may be used. The surgeon may also wish to move to the left side of the table for a short while, to get a more direct look.

PLATE I

A, a midabdominal, right paramedian, muscle retracting (lateral) incision is outlined.

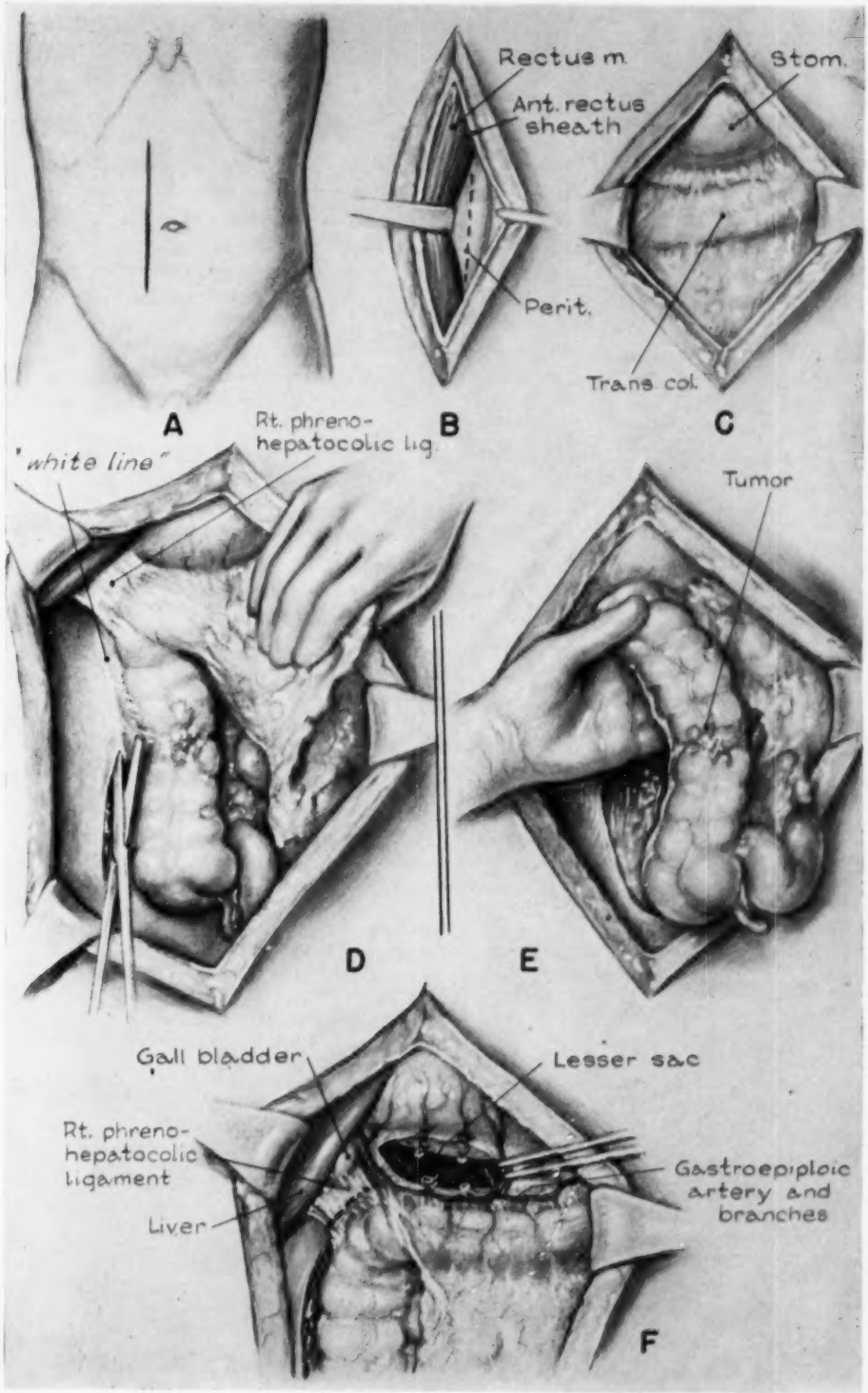
B, the anterior rectus sheath is incised, the rectus muscle is retracted laterally, and the line of incision in the anterior parietal peritoneum is demonstrated.

C, the opening into the peritoneal cavity is completed, and the underlying viscera are depicted.

D, the omentum and small intestines are displaced mesially, and the mobilization of the right side of the colon is commenced by scissor dissection along the fascia-fusion layer of Toldt ("white line").

E, the mobilization of the right side of the colon is continued by digital dissection in the retroperitoneal tissue plane. For purpose of clarity the tumor mass is not covered. Routinely it is encased in a thick, moist gauze pad.

F, the hepatic flexture and the right half of the traverse colon are mobilized by clamping and dividing the right phrenocolic ligament (dotted outline) and the anterior and posterior gastric branches of the gastroepiploic arch respectively. The skeletonization of the distal half of the greater curvature of the stomach is done to include the adjacent gastrocolic ligament and greater omentum in the resected specimen. This insures an adequate removal of the lymphatic drain.


A
Rectus m.
Ant. rectus sheath
Perit.
B
Stom.
Trans col.
C
"white line"
Rt. phreno-hepatocolic lig.
D
Tumor
E
Gall bladder
Lesser sac
Rt. phreno-hepatocolic ligament
Liver
Gastroepiploic artery and branches
F

Warren Cole's work on the danger of implanting tumor cells in the needle-holes of an anastomosis, and also on the possibility of squeezing tumor-cell emboli into the veins during operative handling of the tumor mass, surely deserves further attention and study. Ligation of the bowel (with tape) near either end of the area to be excised, *before* mobilization of the specimen, should make it less likely for the colonic wall at the site of the anastomosis to become coated with desquamated tumor cells that may be implanted by a needle. Similarly, prompt ligation of the right colic vein might theoretically prevent a tumor embolus to the liver. We may eventually know whether these refinements are really worth while.

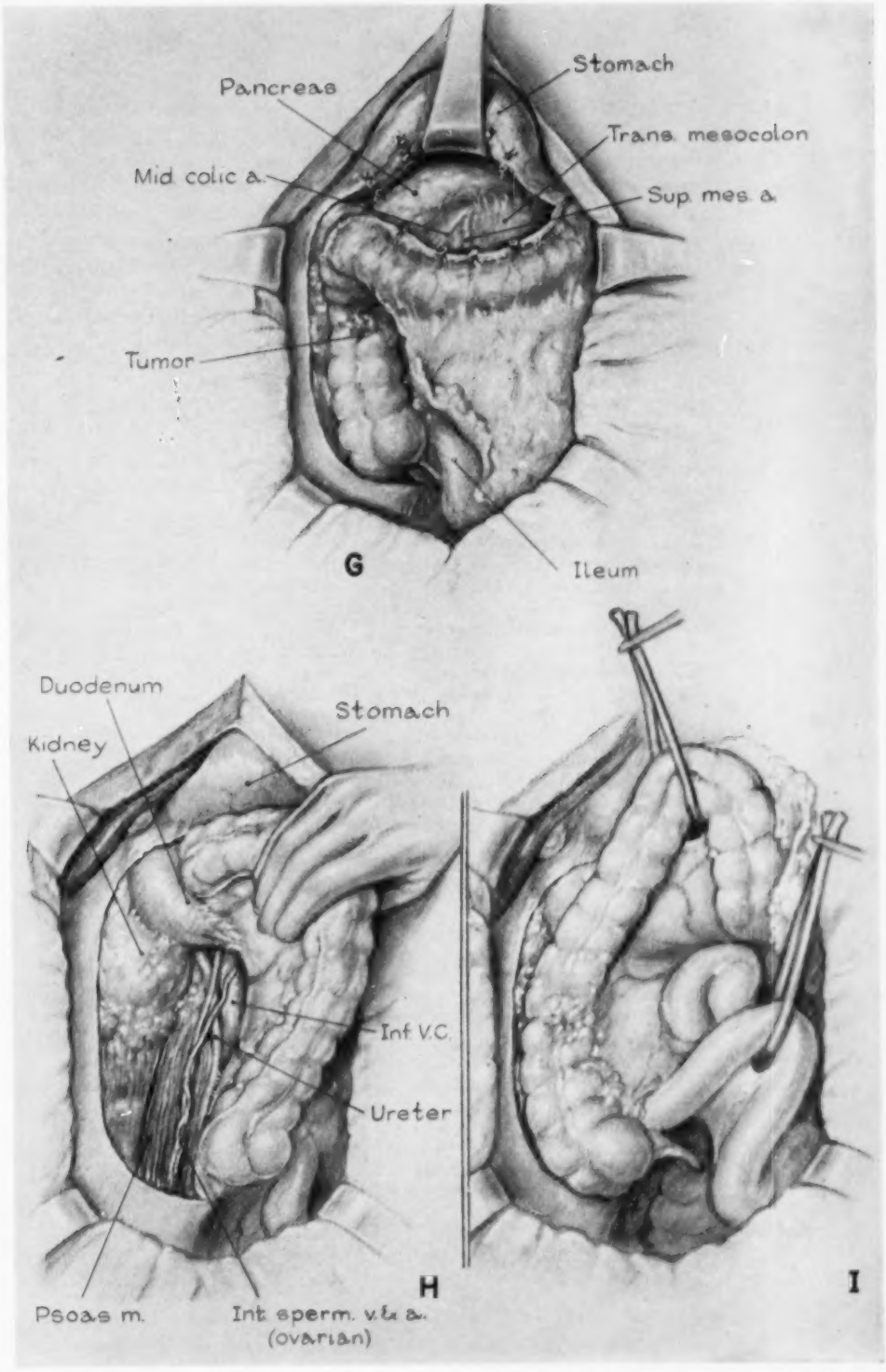
The peritoneum and the thin fascia beneath it form a remarkably good barrier against direct extension, and the retroperitoneal duodenum is very rarely invaded by carcinomas of the right colon, even though they may lie side by side. When this invasion does happen, simple local excision of the obviously involved area of the duodenal wall gives extremely poor results. Hence, a more radical resection of the duodenum should be considered if a cure seems at all possible in any particular case.

PLATE II

G, the mobilization of the right side of the colon and the proximal half of the transverse colon is completed, and the stomach is retracted upward to expose the lesser sac and its related structures.

H, the right side of the colon is retracted toward the midline, and the retroperitoneal structures which are to be identified and protected from injury during the mobilization of the colon are depicted. These structures are (1) the internal spermatic or ovarian vessels; (2) the right ureter; (3) the inferior vena cava; (4) the retrocolic portion of the duodenum.

I, the sites of election for transection of the ileum and transverse colon are encircled by traction tapes of rubber tissue inserted through openings in avascular segments of the mesentery in juxtaposition to the bowel wall.


Pancreas
Stomach
Trans. mesocolon
Mid. colic a.
Sup. mes. a.
Tumor
G
Ileum
Duodenum
Stomach
Kidney
Inf. V.C.
Ureter
H
I
Psoas m.
Int. sperm. v. & a.
(ovarian)

I agree heartily with Dr. Madden's radical approach to the removal of lymph nodes and the right side of the omentum. In this connection, Plate III *J* and *N* and Plate V *Z* are very helpful, though the young surgeon must be warned against too great enthusiasm. It is imperative that the superior mesenteric artery be *most* carefully safeguarded, and the pursuit of enlarged lymph nodes (see Plate III J^1) may lead to damage or angulation of this artery, with subsequent thrombosis. It is well known that the majority of enlarged nodes associated with cancer of the colon turn out to be inflammatory and not neoplastic, and it would be doubly tragic to lose a patient in pursuing these nodes too far. However, this warning should not be misinterpreted as condoning half-hearted attack on the mesentery of the right colon.

PLATE III

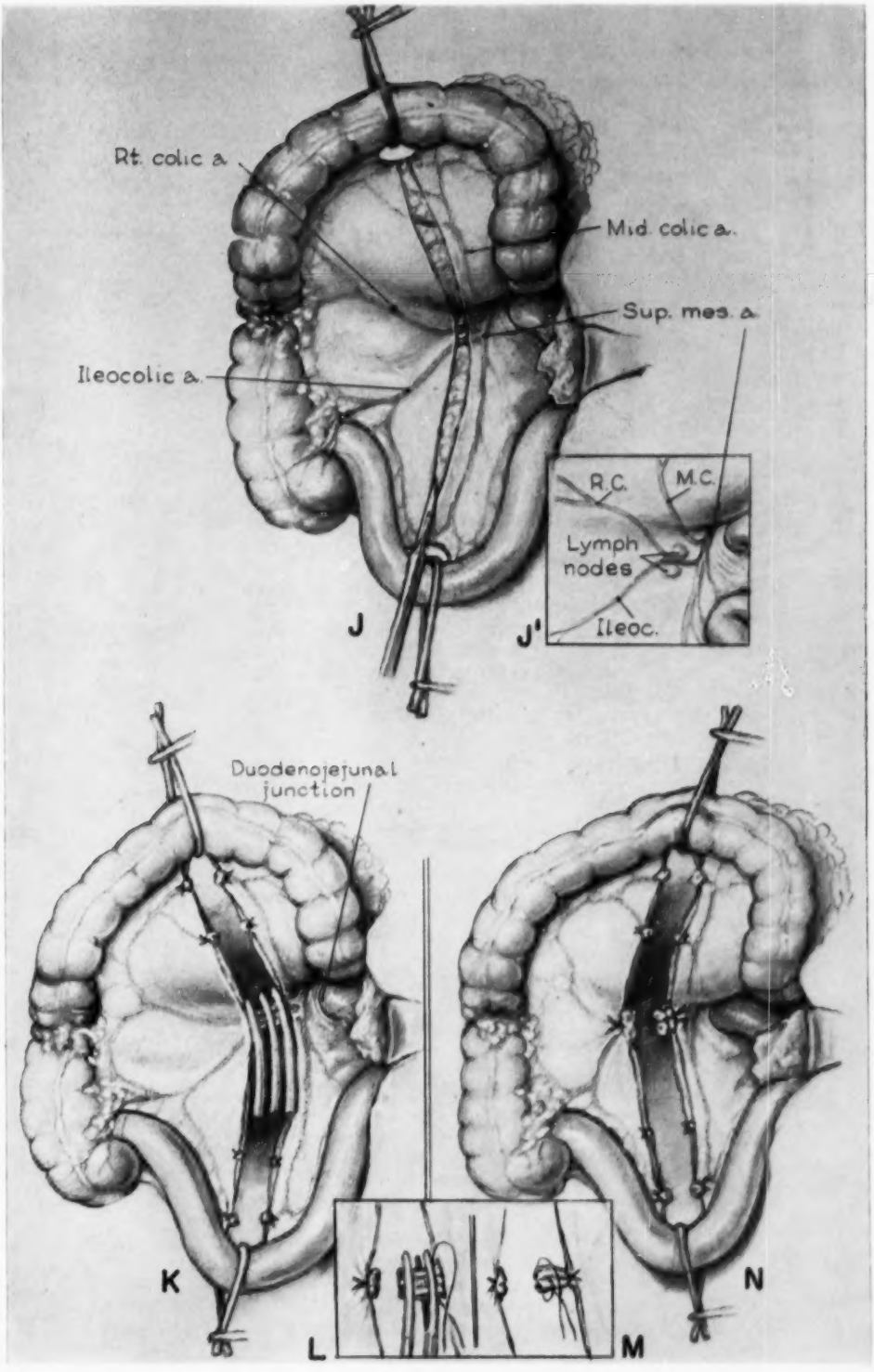
J, incisions, as guide tracts for division of the mesentery, are made through the serosal coverings of the transverse mesocolon and mesentery of the ileum to the respective sites of election for transection of the bowel. The apex of the incisions is at the level of origin of the right colic and/or ileocolic artery.

J^1, inset to show the grouping of the mesenteric lymph nodes about the site of origin of the ileocolic artery from the superior mesenteric artery. Accordingly, in resection of the right side of the colon for carcinoma, the necessity for ligation of the right colic and/or ileocolic artery at their respective levels of origin to include the lymphatic drain is apparent.

K, the division of the mesentery is completed to the level of origin of the right colic and/or ileocolic arteries and hemostasis is obtained with suture ligatures of silk (000). The vascular pedicle is triply clamped prior to division between the two most distal clamps.

L, *M*, insets to show method of occlusion of the vascular pedicle by a proximal ligature and a distal transfixing suture ligature of silk (00).

N, the division of the mesentery of the ileum and the colon is completed, and the isolated ileocolic segment to be resected is demonstrated. For clarity the included segments of greater omentum and gastrocolic ligament are not shown.


Rt. colic a.
Mid. colic a.
Sup. mes. a.
Ileocolic a.
J
R.C.
M.C.
Lymph nodes
Ileoc.
J'
Duodenojejunal junction
K
L
M
N

There is little argument with the choice of end-to-end ileocolostomy as the quickest and best method of restoring continuity at the close of the resection. I have never liked the end-to-side method. At times, in the very old or debilitated patient, I still close both ends and do a side-to-side anastomosis, preferring to have three suture lines that could leak and do *not*, to one that could and *does*. However, the end-to-end method is usually highly satisfactory and is advisable.

PLATE IV

O, noncrushing clamps (Babcock) are used to stabilize the segments of ileum and colon to be anastomosed and crushing clamps are applied to the segments of bowel to be resected. The level of transection of the bowel is in dotted outline. The area of resection includes the terminal 8 to 10 in. of ileum and the proximal portion of the transverse colon up to the site of bifurcation of the middle colic artery into its right and left branches. Routinely the right branch, and not infrequently the whole of the middle colic artery, is included in the resection.

O^1, inset to show a close up of the mesenteric coapting suture of Lee.

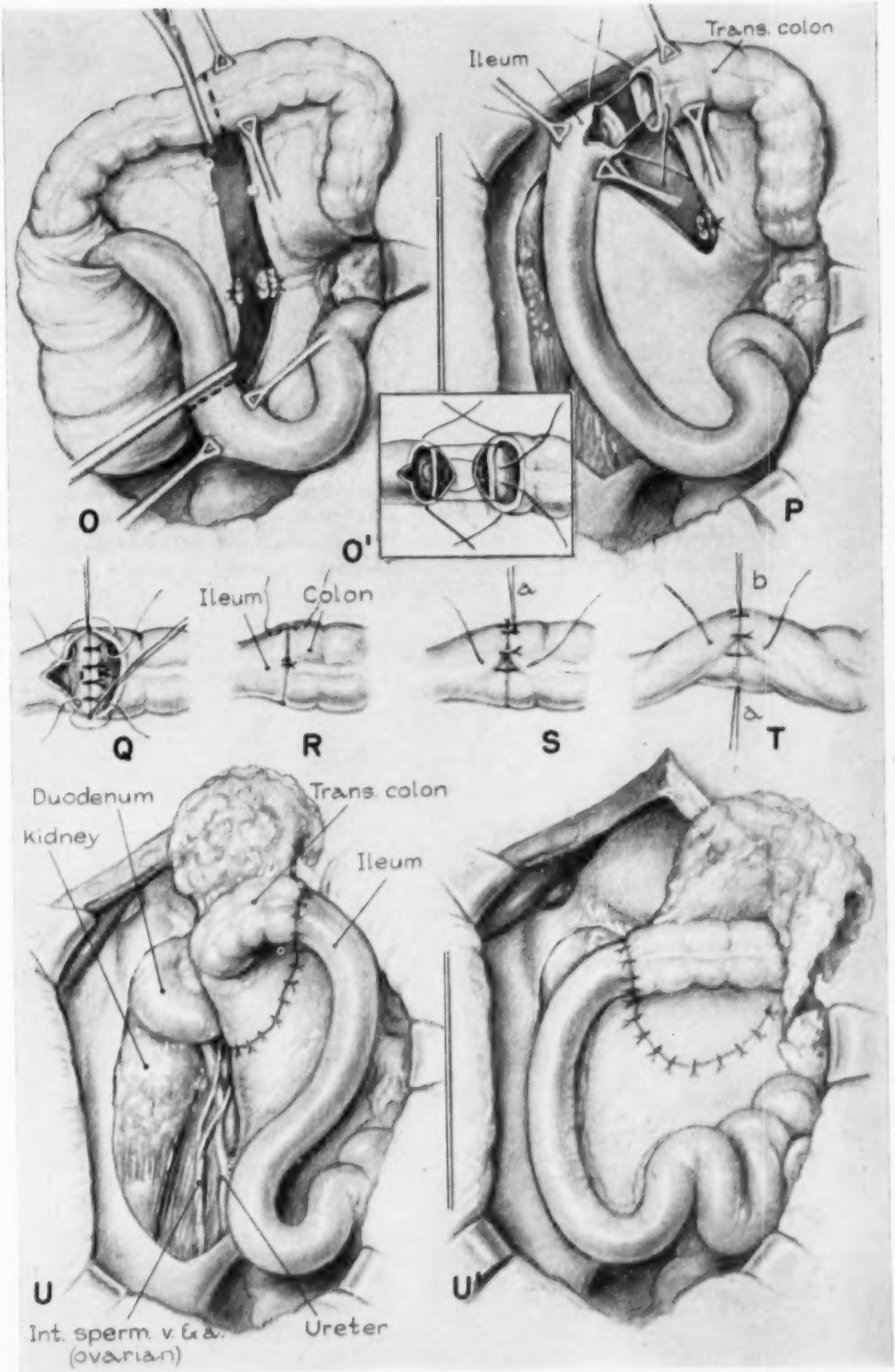
P, guy sutures of silk are inserted through the lateral margins of the bowel wall, and the ileum is split along its antimesenteric surface to enlarge the diameter of its lumen at the site of anastomosis.

Q, the first posterior layer of the anastomosis is completed, and the first anterior layer is commenced. The central mattress suture for coaptation of the mesentery is visible. The sutures anteriorly are inserted from the "inside out" to the "outside in" so that when the knots are tied they are on the inside of the lumen. Interrupted sutures of silk (000) are used throughout.

R, the first anterior inversion layer is completed, and the second anterior layer of seroserosal sutures (Lembert) is begun. A figure-of-eight mattress suture indicates the termination of the closure in the center of the first anterior layer.

S, *T*, completion of the second layer of sutures anteriorly and the rotation of the bowel on its long axis to complete the second layer posteriorly.

U, U^1, the completed end-to-end ileotransverse colon colestomy and the approximation of the mesenteric borders viewed from behind and in front respectively. No attempt to reperitonize the denuded area along the right posteriolateral abdominal wall is made. Closure of the opening in the mesentery both anteriorly and posteriorly, as depicted, is not required.


Trans. colon
Ileum
O
O'
P
Ileum
Colon
a
b
a
Q
R
S
T
Duodenum
Kidney
Trans. colon
Ileum
U
U'
Int. sperm. v. & a.
(ovarian)
Ureter

Peritonization of the posterior raw surface is usually difficult. I do not attempt it and have never had any reason to regret not doing so.

The matter of establishing drainage is highly controversial. Multiple soft rubber drains may be brought out through a small flank incision and placed to the raw area. I am likely to use drainage in an obese patient, especially if the operation has been long and difficult, or there has been much inflammatory reaction in and about the tumor. This is not in anticipation of a leak at the suture line (fortunately, very rare) but to get rid of some contaminated bloody fluid. However, this is probably an unnecessarily conservative approach, now that preoperative preparation of the colon is so greatly improved.

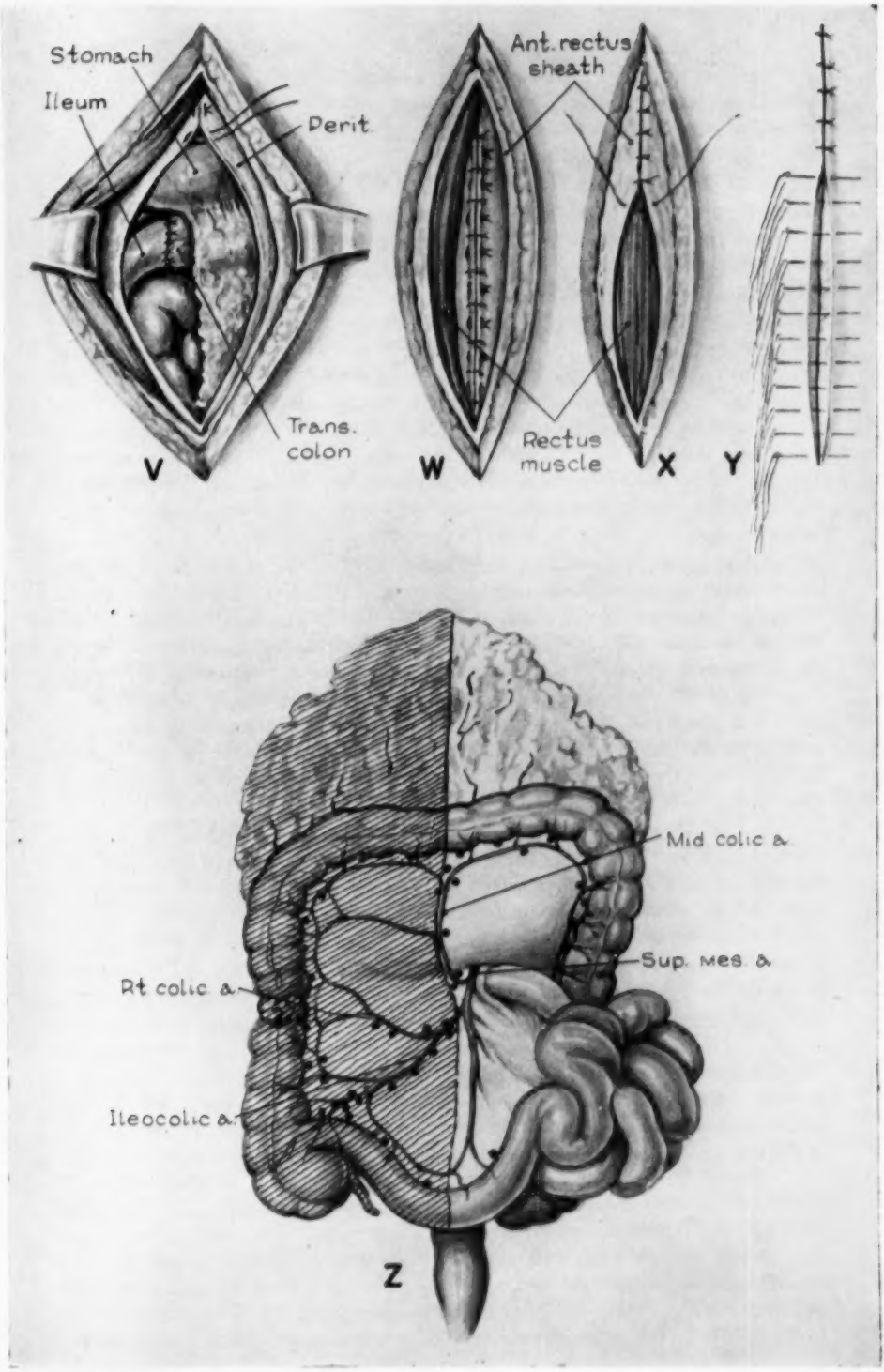
PLATE V

V, W, the approximation of the peritoneal layer with interrupted everting mattress sutures of silk (00) alternating with simple interrupted sutures is shown.

X, Y, the fascial layer and skin are approximated with interrupted sutures of silk (00). In the closure of the skin the needles are first inserted, individually withdrawn, and the sutures tied.

Z, diagrammatic representation of the extent of bowel resection in the performance of a right hemicolectomy for carcinoma involving the right side of the colon.

Roosevelt Hospital.


Stomach
Ileum
Perit.
Trans. colon
V
Ant. rectus sheath
Rectus muscle
W
X
Y
Mid colic a.
Sup. mes. a.
Rt colic a.
Ileocolic a.
Z

Editorials

Benjamin Franklin

During the year of 1956 many organizations as well as nations paid tribute to Benjamin Franklin on the 250th anniversary of his birth. It is quite fitting that the medical profession pause and acknowledge its debt to his genius.

The manifold benefits in our daily lives directly and indirectly attributable to him are incalculable. His numerous interests and the many facets of his colorful life have kept biographers busy for years. His role as a scientist with many publications, as our first ambassador to France, as our first postmaster general, and as a stateman in the history of our country and England is not fully realized nor appreciated today. The Revolutionary War could have been avoided, according to some authorities, if Franklin's advice in the Albany Plan of 1754 had been adopted. The War Between The States nearly 100 years later, and our current problem of segregation, probably never would have occurred if his counsel had but been heeded.

The medical interests of Benjamin Franklin encompassed a wide range. His knowledge of the common cold was as great, or small, as our own today. Interestingly, he mentioned in 1773 that the disease had been called "a cold" by the English for about 150 years. From his own experiments on humans he wrote on the therapeutic effects of electricity on paralytics in Pennsylvania. He was a shrewd observer. "I never knew any advantage from Electricity in palsies that was permanent. And how far the apparent temporary advantage might arise from the exercise in the patient's journey, and coming daily to my house, or from spirits given by the hope of success, enabling them to exert more strength in moving their limbs, I will not pretend to say."

Franklin's experiments in hypnotism antedated even the birth of the original "Bridey Murphy," and he was influential in discouraging the use of hypnotism and mesemerism as a cure-all in France. He planned and fostered the Academy of Pennsylvania, which grew into the College of Philadelphia. His enthusiasm and power of promotion were largely responsible for the founding of the Pennsylvania Hospital. As president of the board of trustees of the University of Pennsylvania he signed the "Rules Respecting a Medical Education and a Degree."

In 1772 Benjamin Franklin's oldest brother John was having some difficulty voiding. Thereby the first flexible catheter in this country was designed by Franklin, paving the way for a specialty for our urological brethen. Franklin's letter to John is preserved today and is written in beautiful eighteenth century script. Although two years was the total of his formal education, he was steeped in the writings of Addison and Steele. The music of his opening phrase displays this influence. "Reflecting today on your desire to have a flexible catheter, a thought struck into my mind how one might properly be made . . . ." As in his invention of bifocal glasses, his mechanical genius is displayed again in the thought that "struck into his mind." If we today pause to reflect how we would design a flexible catheter without the use of rubber or gutta percha, we realize that our ingenuity would be taxed in spite of modern technology. Franklin simply had his silversmith twist fine wire into a spiral and covered it with small cleaned animal

intestine. He evidently avoided testing it on himself before posting it on the next stage to brother John. "I think it is as flexible as would be expected in a thing of the kind, and I imagine will readily comply with the turns of the passage, yet has stiffness enough to be protruded; if not, the enclosed wire may be used to stiffen the hinder part of the pipe while the fore part is pushed forward."

Thirty years later Benjamin himself was troubled with a bladder stone that bothered him the rest of his life. It eventually became so painful that he could not bear the jolt of his carriage over the pavement. After returning to France from America in 1778, he developed "the scurf extending all the small of my back, on my sides, my legs and my arms, besides what continued under my hair." This may have been psoriasis. He was also troubled with gout and wrote a humorous "Dialogue Between Franklin and the Gout." At 75 years of age he remembered a song, and old favorite sung so often in his youth,

> May I govern my passions with absolute sway,
> Grow wiser and better as my strength wears away,
> Without gout or stone, by a gentle decay.

Comments he, "I now find at four score that the three contraries have befallen me, being subject to the gout and the stone, and not yet master of all my passions."

Nine days before his death, in 1790 at 84 years of age, with his mental faculties intact, he wrote his last of many thousand letters. It was to Thomas Jefferson, clearly and accurately telling of the map used in fixing the boundary between Maine and Nova Scotia. Dr. Benjamin Rush, the only physician to sign the Declaration of Independence, wrote of Franklin's death. "He rose from his bed and begged that it be made up for him so he might die in a decent manner. His daughter told him that she hoped he would recover and live many years longer. He calmly replied: 'I hope not'."

Years before, Franklin had expressed himself in a letter of condolence to his niece, the daughter of his brother John. "A man is not completely born until he be dead. Why then should we grieve that a new child is born among the immortals, a new member added to their happy society."

Two centuries later, appreciating the man as well as his deeds, biographer Carl Van Doren aptly epitomizes, "his achievements were less than he was. Whoever learns about his deeds remembers longest the man who did them. . . . He seems to have been more than any single man: a harmonious human multitude."

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Case Reports

Benign Leiomyoma of Jejunum

Report of Two Cases

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Montgomery, Ala.

Massive bleeding from the gastrointestinal tract has posed a real problem in diagnosis and treatment where the underlying cause has been obscured. We have successfully treated two such cases due to leiomyomas of the jejunum.

Much has been written on the subject of smooth-muscle tumors, but there is still some confusion, and this results in an incorrect diagnosis and a plan of treatment not always the most desirable.

Golden and Stout have reported 60 smooth-muscle tumors of the gastrointestinal tract at the Presbyterian Hospital, New York. There were 50% of these cases that caused symptoms, and they were distributed as follows: stomach 27%, duodenum 7%, jejunum 3%, ileum 10%, Meckel's diverticulum 3%, colon 7%, rectum 16%, retroperitoneal 27%. Thus it is seen that leiomyomas of the jejunum and Meckel's diverticulum are the rarest but actually a frequent cause of massive obscure gastrointestinal bleeding.

Pathology

These tumors are indurated, rounded, well-defined, and often pedunculated. The tumors originate in the muscularis and may extend submucosally or subserosally or in both directions. They usually ulcerate through the mucosa and bleed into the lumen of the gastrointestinal tract.

Histologically they fall into the classification of smooth-muscle tumors elsewhere in the body. The tumor may show well-differentiated muscle cells, but the malignant type shows many atypical shorter cells, irregular forms, poor organization, and mitotic figures. Golden and Stout have concluded that if two or more mitoses per high-power field are present one can feel fairly secure in predicting malignancy.

Symptoms

Symptoms usually are vague and, according to Schindler et al., the presenting symptom is blood loss—either anemia, hematemesis, or melena. Leiomyomas of the jejunum notoriously bleed, although partial, slowly developing intestinal obstruction due to gradual encroachment on the lumen by the submucosal type has been noted. Gastrointestinal x-ray series are of no value in diagnosis of this lesion.

In view of the rare occurrence of this lesion and its relatively frequent cause of obscure massive gastrointestinal bleeding, the following report of two cases is added to the literature.

Report of Cases

CASE 1.—A man was admitted to the hospital for the fourth time, Jan. 3, 1956, with a chief complaint of tarry stools. The patient was previously hospitalized here June 10, 1955, and again Nov. 22, 1955, each time with tarry stools but no history of hematemesis. The gastrointestinal hemorrhages have been massive on occasions and have required transfusions. On Nov. 22, 1955, the red blood cell count was 2,630,000 and hemoglobin level was 7 gm. During this admission the patient was given several transfusions.

Submitted for publication Sept. 18, 1956.
From the Veterans Administration Hospital.

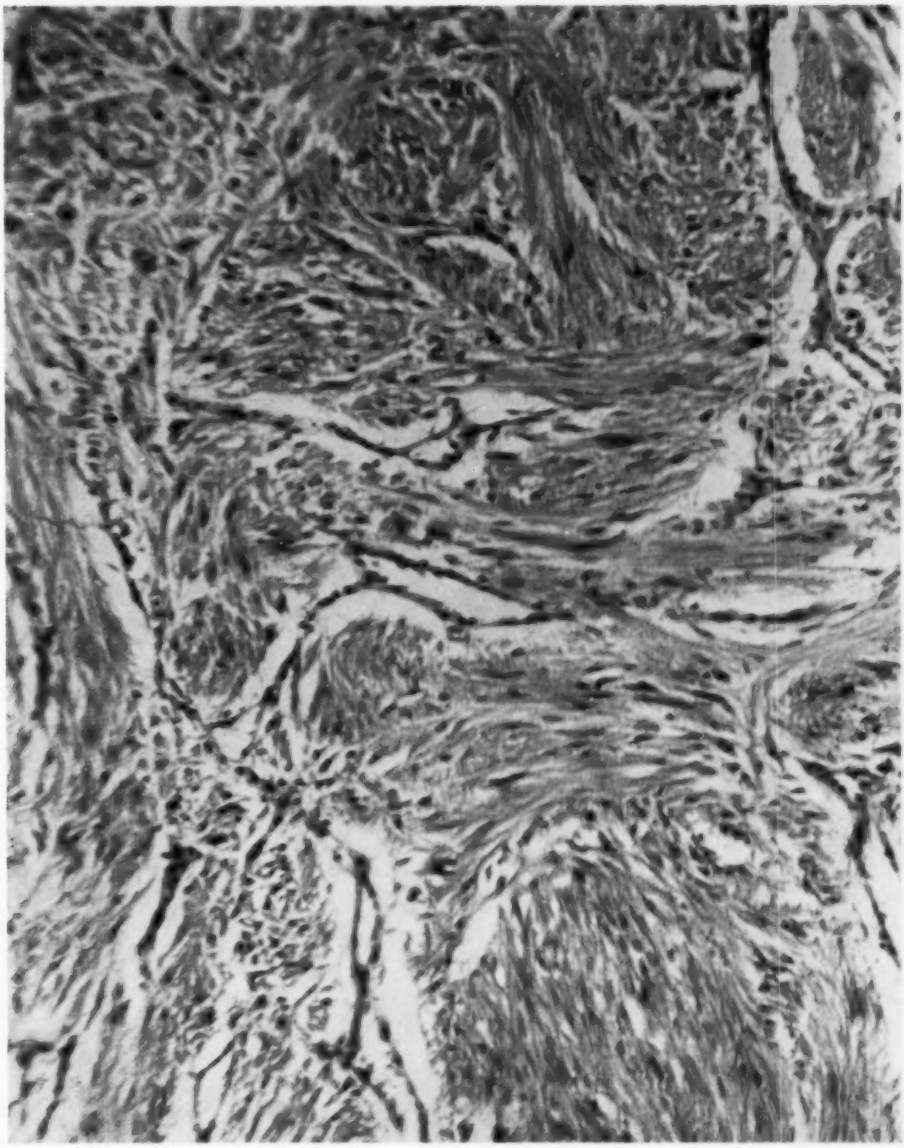

Fig. 1.—Microscopic. Section shows a portion of small intestine in which there is a tumor of the muscle layer which protrudes in an hourglass character into the submucosa and serosal layer. It is composed of spindle cells which show interlacing bundles. It apparently has arisen in the smooth muscle. No evidence of any nerve component is present. There is no evidence of mitotic activity or malignant change.

Physical examination revealed a tall, thin, white man who did not appear acutely ill. Blood pressure was 170/90. Funduscopic examination showed Grade II vascular changes.

Laboratory work-up revealed a red blood cell count of 2,700,000 and hemoglobin of 9 gm.; hematocrit 26%. The total serum proteins was 5.6 gm. per 100 cc.

X-ray of the chest on Jan. 10, 1956, was reported as follows: "There is tortuosity of the thoracic aorta as may be associated with hypertension or arteriosclerosis." X-ray barium enema report made

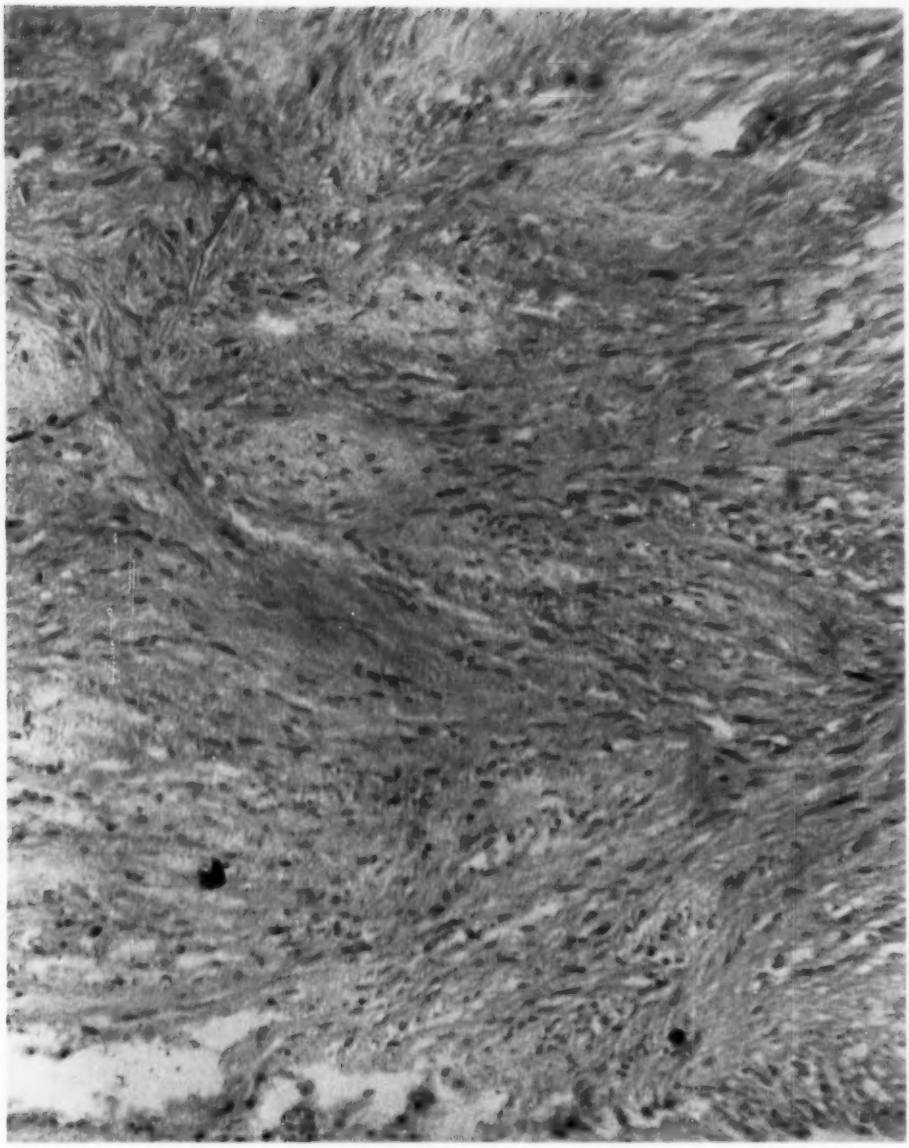

Fig. 2.—Microscopic. Section shows a tumor composed of spindle cells in which the cells are quite regular in size, shape, and staining. They show interlacing bundling. No evidence of mitosis or malignancy is present. It is felt that this is a leiomyoma from the wall of the small intestine. It is histologically benign. Also present is a portion of mucosa from the intestine in which there is no evidence of tumor.

on May 31, 1955, admission read as follows: "There are a number of diverticula in the region of the descending colon and sigmoid."

A gastrointestinal x-ray series made on Nov. 29, 1955, admission was reported as "negative."

Electrocardiographic tracings made on May 20, 1955, and Nov. 23, 1955, were reported as "abnormal and suggestive of myocardial ischemia."

Prior to surgery the patient was prepared with repeated transfusions, and on Jan. 16, 1956, an

Fig. 3.—Gross. The formaldehyde (Formalin)-fixed specimen consists of a previously opened segment of bowel 7 cm. in length and 6 cm. in circumference. In the center of the specimen is a tumor mass which is dumbbell in shape and present in the submucosa and the subserosa. The subserosal section measures 3 cm. in diameter and that within the submucosa, 1.8 cm. The mucosa over the tumor shows a tiny area of ulceration. The tumor is fleshy and moderately firm. Submitted separately is a portion of bowel 3 cm. in length and 3 cm. in diameter. In the submucosa at one end is a small amount of hemorrhage.

exploratory laparotomy was performed with the patient under general anesthesia. The source of the gastrointestinal bleeding was found to be a tumor of the jejunum approximately 3 in. distal to the ligament of Treitz. The lesion was resected and an end-to-end anastomosis of the jejunum was done. Following this procedure the patient had a normal convalescence. Microscopic examination of the tumor was reported as leiomyoma of the jejunum (Figs. 1 and 2).

This patient returned to the hospital on Feb. 29, 1956, for follow-up examination. At this time he was asymptomatic, had gained 6.7 kg. (15 lb.) in weight, and had had no further bleeding.

The patient was instructed to return in six months for evaluation.

Case 2.—A Negro man was admitted to the hospital for the first time on May 15, 1956, with a chief complaint of tarry stools which he had had intermittently for the past one and one-half years. Six days prior to admission the patient took a dose of castor oil, which was followed by rectal bleeding of bright-red blood. Following this he had an attack of syncope. The patient had never vomited blood. His admission complaint has been accompanied by left-flank pain, weakness, and anorexia for three to four years.

Physical examination revealed a 64-year-old thin Negro man who appeared chronically ill. The blood pressure was 112/60. Arcus senilis was present.

Laboratory work-up revealed red blood cell count 1,520,000, hemoglobin level 4.5 gm., total serum protein 6.15 gm/100 cc., serum albumin 3.21 gm/100 cc.

X-ray of the chest and a scout film of the abdomen showed no abnormality.

Prior to surgery the patient was prepared with repeated transfusions. On May 18, 1956, a proctosigmoidoscopic examination failed to reveal the cause of bleeding. On May 21, 1956, a laparotomy was performed with general anesthesia. A tumor was found on the antimesenteric side of the jejunum about 90 cm. from the ligament of Treitz. The lesion was resected and an end-to-end anastomosis performed.

The postoperative course was uneventful, the patient being discharged on the 15th postoperative day.

John Templeton, from the Illustration Laboratory, VA Hospital, supplied the radiographs and photomicrographs.

Veterans Administration Hospital.

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Hormonally Influenced Hemangioma

SCOTT J. BOLEY, M.D., and WILLIAM E. MORSE, M.D., Brooklyn

The growth of vascular tumors in response to hormonal stimulation is a well-documented and generally accepted fact. The development of nevus-araneous-like hemangiomata associated with the high hormonal blood levels of pregnancy has been described by Walsh and Becker, Forman, Zeisler, Feldman, and others.

The "pregnancy tumor," frequently mentioned in the dental literature and described by Thoma and Miller as a fibroangioma or a form of epulis, is another example of the growth of vascular elements in response to rising hormonal titers. Neither the telangiectasis nor "pregnancy tumors" are true neoplasmas, but they do represent cyclic hyperplasia of vascular tissues.

The effect of endocrine stimulation on cavernous hemangiomas, true neoplasmas, in contradistinction to the aforementioned hyperplasias, remains a controversial issue. Although Kitlowski has described flare-ups of these tumors at the time of puberty and of menopause and during pregnancy, Johnson, Ghormley, and Dockerty in a recent review of hemangiomas of the extremities at the Mayo Clinic found no evidence to support this hypothesis. However, these authors did not exclude the possibility of hormonal influence on arteriolar growth and proliferation as a factor in the spontaneous growth of these tumors.

Lam, in 1951, and Mackles, in a personal communication to us, reported two cases in which growth of a hemangioma during pregnancy produced central nervous system changes. These symptoms were due to pressure on the spinal cord from enlargement of a cavernous hemangioma.

The purpose of this paper is to present a case of cavernous hemangioma with apparent cyclic growth associated with the onset of lactation in the postpartum period. We feel it is unique in that we have been unable to find any previous reference to stimulation of hemangioma coinciding with the rise and fall of the lactogenic hormone levels.

Report of Case

A 26-year-old Negro woman, gravida 3 para 2, was admitted to the obstetrical service of the Jewish Hospital of Brooklyn in February, 1956, in the 40th week of a normal gestation. On Feb. 2, 1956, the patient had a normal, full-term, spontaneous delivery. Two days later, concomitant with painful swelling of her breasts, the patient noticed a painful swelling over her left thenar space. Physical examination at this time revealed a firm, 2 by 4 cm. mass, bluish in color and tender to palpation (Fig. 1). X-rays of the hand were negative.

Past history revealed that in September, 1954, following the patient's second pregnancy and coincidental with painful engorgement of her breasts, this same symptomatic tumefaction was noted. Further, with cessation of lactation the mass disappeared, and the patient remained asymptomatic until this time. No similar occurrence was reported after her first gestation in 1953.

On March 2, 1956, surgery was performed and a well-encapsulated, dark bluish-red, spongy tumor 2 by 4 cm. was excised. This tumor lay deep to the skin of the left thenar space and grossly had the typical characteristics of a cavernous hemangioma (Fig. 2). Microscopic examination confirmed the diagnosis (Fig. 3). The postoperative course has been uneventful.

Comment

The cyclic appearance, regression, and reappearance of the tumor in this case

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From the Department of Surgery, Jewish Hospital of Brooklyn.

Fig. 1.—The tumefaction overlying the left thenar space is easily seen. The engorgement of the breasts coincidental with which the mass in the hand appeared is also shown.

Fig. 2.—The tumor has the typical gross appearance of a hemangioma. The vascular pedicle is seen at the lower left aspect of the specimen.

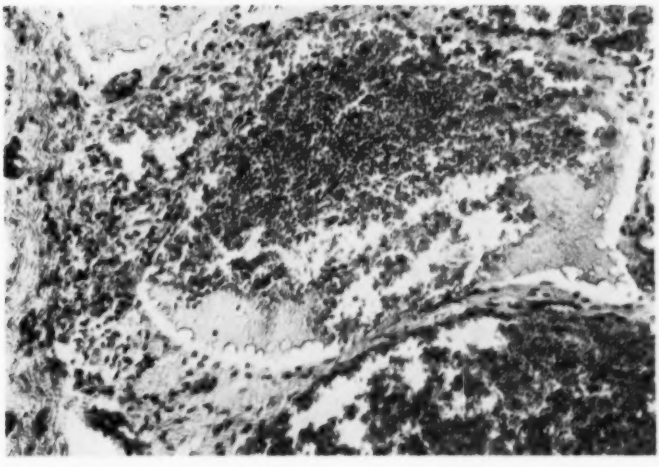

Fig. 3.—The blood-filled, endothelial lined, cavernous spaces are characteristic of a cavernous hemangioma.

leaves little room for doubt as to its response to some hormonal stimulus. If one accepts the patient's history, the apparent growth of the hemangioma with the onset of lactation points to the so-called "lactogenic hormone" as the responsible endocrine factor. Certainly the failure of the tumor or the symptoms to become manifest prior to delivery excludes stimulation by the hormones of normal gestation.

Although hemangioma was mentioned in the differential diagnosis, the most probable diagnosis preoperatively was felt to be ectopic breast or endometrial tissue. The basis for this assumption was the known response of these tissues to hormonal stimulation. This case bears out previous reports that cavernous hemangiomas can similarly respond to cyclic endocrine titers and regress completely upon withdrawal of the responsible hormone.

Summary

The problem of the growth response of vascular tumors to hormonal stimulation is discussed, and the literature is reviewed. A case of a cavernous hemangioma which demonstrated definite growth and disappearance associated with the onset and cessation of lactation is presented.

Jewish Hospital of Brooklyn.

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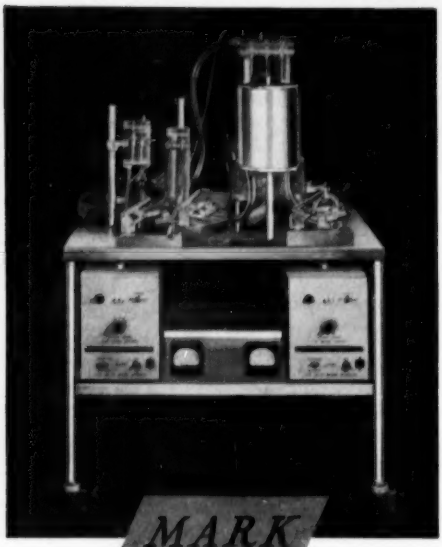

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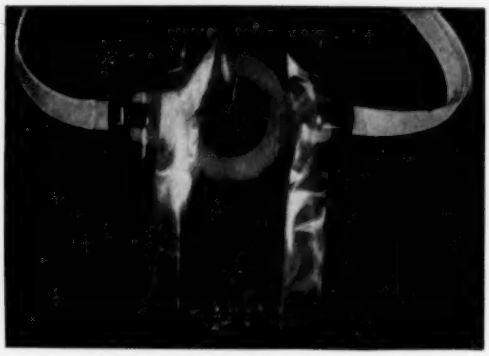

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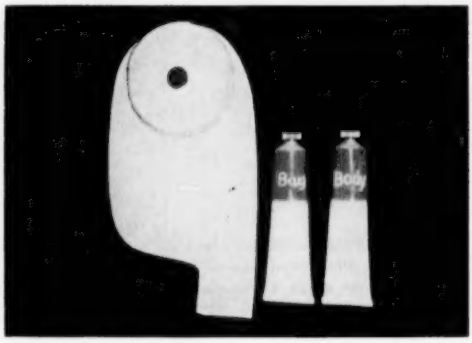

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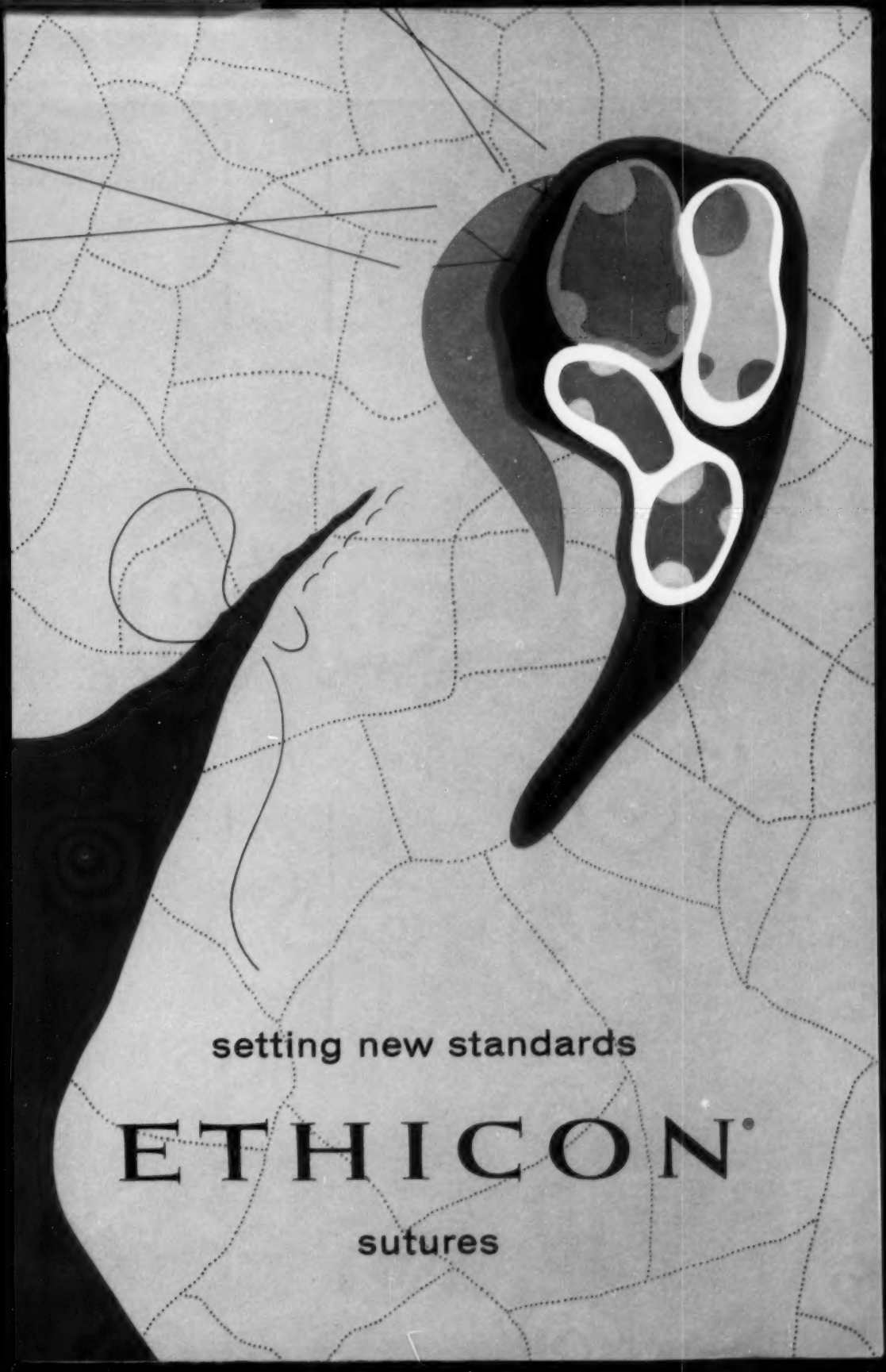
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